REMARKS

Claims 1-20 are pending in the application. Claims 1-15 and 17-20 are cancelled, without prejudice. New Claims 21-25 are added and Claim 16 is amended. Support for new Claims 21-25 can be found, e.g., in originally filed Claim 12. In particular, support for Claim 21 can be found, e.g., on page18, lines 5-14, and on page 62, lines 33-36. Applicants reserve the right to prosecute the subject matter of Claims 1-11, 19, and 20 in subsequent divisional applications. The Specification is amended to provide a more descriptive title, update the patent family status of the present application, and eliminate browser-executable codes.

Applicants believe no new matter is added by the foregoing amendments.

I. Objections and Informalities

The Examiner objected to the title as not being descriptive of the present invention. Applicants have amended the title accordingly. The Examiner further requested that the patent family status be updated. Applicants have amended the specification to incorporate the proper priority information. The Examiner objected to the Specification for containing browser-executable codes. Applicants have amended the Specification to refer to the websites by a non-executable name.

The Examiner found the present application lacking an abstract. According to the date stamped return receipt postcard (a copy of which accompanies this response), the USPTO received an abstract with the original filing papers. For the Examiner's convenience a copy of the original abstract is enclosed.

In view of the above, Applicants believe that the grounds for these objections have been obviated. Withdrawal of these objections if respectfully requested.

II. Objections to Claims 12 and 16

The Examiner objected to Claims 12 and 16. Claim 12 was objected to as depending from a non-elected claim. Claims 12 and 16 were also objected to as reciting non-elected inventions. Claim 12 is canceled and the objections are therefore moot as to this claim. Claim 16, as amended, no longer recites non-elected inventions. Applicants respectfully request withdrawal of the objections to Claims 12 and 16 in view of the above amendments.

III. Rejection of Claim 12 under 35 U.S.C. 112, Second Paragraph

The Examiner rejected Claim 12 under 35 U.S.C. 112, second paragraph, for indefiniteness. Claim 12 is canceled and the rejection is therefore moot as to this claim. Applicants believe that new Claims 21-25 are free from this rejection.

In view of the above, Applicants respectfully request withdrawal of this rejection.

IV. Rejections of Claims 12-18 under 35 U.S.C. §101

The Examiner rejected Claims 12-18 under 35 U.S.C. §101 alleging that the present invention lacks specific, substantial, and credible utility. Claims 12-15 are canceled and the rejection is therefore moot as to these claims. To satisfy the utility requirement, applications must contain a credible asserted utility that is specific to the subject matter of the invention and involves a "real world" use. Credibility of the asserted substantial and specific utility is judged according to that which ". . . would be considered credible by the person of ordinary skill in the art" (In re Rinehart 531 F.2d 1048,1052, 189 USPQ 142, 147 (CCPA 1976)).

The Examiner is directed to page 22, lines 6-7, where the Applicants asserted utility for the present cytokine receptor is ". . . modulation of an inflammatory function . . .". This asserted specific and substantial utility is further supported on page 68, lines 29-34, of the specification, where expression of the present invention appears in several in vitro models of the inflammatory state, e.g., activated dendritic cells.

In further support of this asserted utility, Applicants are able to submit extraneous evidence of utility via printed publications as put forth in M.P.E.P 2107.2(VI). Blumberg, et al. (2001) Cell 104:9-19, demonstrates the elevated expression of DIRS1 (a.k.a. IL-20Rβ) in psoriasis, an inflammatory skin disorder. Blumberg also puts forth evidence receptor signaling when bound by the ligand, IL-20, which is also implicated in various inflammatory skin disorders. Dumoutier, et al. (2001) J. Immunol. 167:3545-3549 further demonstrates that the binding of IL-20 to DIRS1 and another subunit, IL-20Rα, results in STAT activation, as well as the implication of the ligand and receptor complex in inflammatory skin disorders.

WO 01/46232, published June 28, 2001, associates the receptor of the present invention, DIRS1 or IL-20Rβ, with another subunit, IL-20Rα, and demonstrates upregulation of the receptor construct psoraisis (see, e.g., page 36, Example 10).

Taken together, Applicants submit that the asserted utility in the present specification is substantial, specific, and credible to the skilled artisan. In view of the above, Applicants respectfully request that the rejection of Claims 12-18 under 35 U.S.C. 101 be withdrawn.

V. Rejection of Claims 12-18 under 35 U.S.C. 112, First Paragraph

The Examiner rejected Claims 12-18 under 35 U.S.C. 112, first paragraph, on the basis that ". . . since the claimed invention is not supported by either a specific and substantial asserted utility . . . one skilled in the art clearly would not know how to use the claimed invention" (Office Action, page 8). Claims 12-15 are canceled and the rejection is therefore moot as to these claims. As noted above, the present invention is supported by a credible, substantial, and specific utility, e.g., modulation of inflammatory responses. Therefore one skilled in the art would, in fact, know how to use the present invention.

The Examiner further alleges that the specification does not enable polypeptide or polynucleotide variants as recited various subsections of Claims 12, 16, and 17, as well as Claims 13-15. Claims 12-15 and 17 are canceled and the rejection is therefore moot as to these claims. The Examiner alleges that the present specification does not provide guidance with regard to the production of fragments having identity to SEQ ID NO:1. As amended Claim 16 does not recite fragments nor do new Claims 21-25.

In view of the foregoing, Applicants submit that the rejection of Claims 12-18 is overcome. Withdrawal of this rejection is respectfully requested.

Conclusion

Applicants' current response is believed to be a complete reply to all the outstanding issues of the latest Office Action. Further, the present response is a bona fide effort to place the application in condition for allowance or in better form for appeal. Accordingly, Applicants respectfully request reconsideration and passage of the amended claims to allowance at the earliest possible convenience. Should the Examiner deem allowance inappropriate at this time, Applicants respectfully request an interview be granted with the undersigned to consider any issues.

Respectfully submitted,

Date: April 19, 2002

Sheela Mohan-Peterson
Reg. No. 41,201
Attorney for Applicants

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901 California Avenue
Palo Alto, California 94304-1104
Tel: (650) 496-1244
Fax: (650) 496-1200

Attachments:
(A) Blumberg, et al.
(B) Dumoutier, et al.
(C) WO 01/46232
(D) Copy of Return Receipt Postcard
(E) Copy of Abstract as filed

(F)

VERSIONS WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The paragraph on page 70 (lines 22-27) has been amended as follows:

The cellular forms of receptors for ligands can be tested with the various ligands and receptor subunits provided, e.g., IL-10 related sequences. In particular, multiple cytokine receptor like ligands have been identified, see, e.g., [USSN 60/027,368, 08/934,959, and 08/842,659] and U.S. Patent No. 5,989,867 issued to Knappe, et al., which are incorporated herein by reference[.].

The paragraph beginning on page 27 (lines 17-37) and concluding on page 28 (lines 1-9) has been replaced with the following paragraph:

Another example of an algorithm that is suitable for determining percent sequence identity and sequence similarity is the BLAST algorithm, which is described Altschul, et al. (1990) J. Mol. Biol. 215:403-410. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information [(http:www.ncbi.nlm.nih.gov/)] on the world wide web at "ncbi.nlm.nih.gov." This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul, et al., supra). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are then extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the

alignment. The BLAST program uses as defaults a wordlength (W) of 11, the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1989) Proc. Nat'l Acad. Sci. USA 89:10915) alignments (B) of 50, expectation (E) of 10, M=5, N=4, and a comparison of both strands.

In the Claims

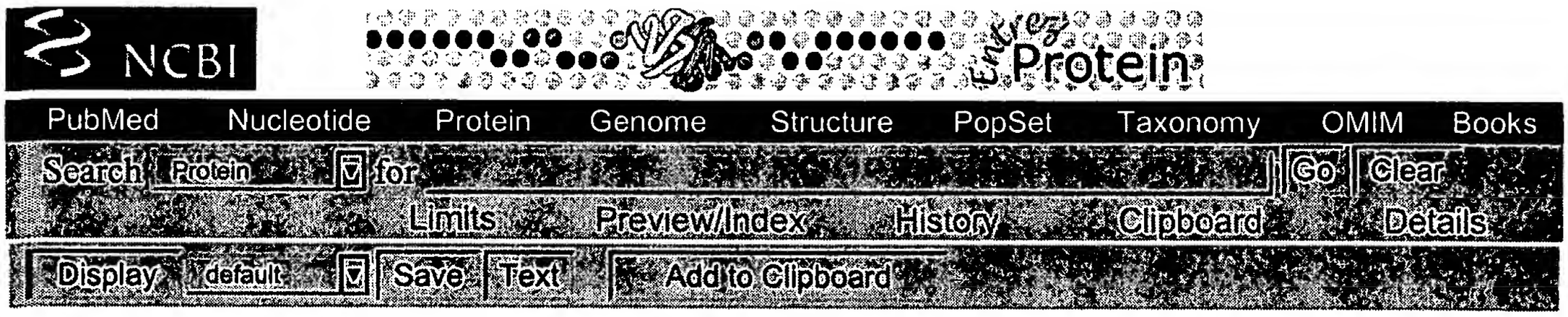
16. (Amended Once) A nucleic acid which[:

a)]hybridizes under wash conditions of 30 minutes at [30] 55° C and [less than 2M] 150mM salt to the coding portion of SEQ ID NO: 1[;

[b) hybridizes under wash conditions of 30 minutes at 30° C and less than 2M salt to the coding portion of SEQ ID NO: 3; or

c) exhibits identity over a stretch of at least about 30 nucleotides to a primate DIRS1; or

d) exhibits identity over a stretch of at least about 30 nucleotides to a primate DIRS2].



1: NP_653318. hypothetical prot...[gi:21389499]

BLink, Nucleotide, Related Sequences, Taxonomy, LinkOut

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LOCUS       MGC34923                  169 aa            linear   PRI 11-JUN-2002
DEFINITION  hypothetical protein MGC34923 [Homo sapiens].
ACCESSION   NP_653318
VERSION     NP_653318.1  GI:21389499
DBSOURCE    REFSEQ: accession NM_144717.1
KEYWORDS    .
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (residues 1 to 169)
  AUTHORS   Strausberg,R.
  TITLE     Homo sapiens hypothetical protein MGC34923 (MGC34923), mRNA
  JOURNAL   Unpublished (2002)
COMMENT     PREDICTED REFSEQ: The mRNA record is supported by experimental
            evidence; however, the coding sequence is predicted. The reference
            sequence was derived from BC027449.1.
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                     /db_xref="taxon:9606"
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                     /clone_lib="NIH_MGC_12"
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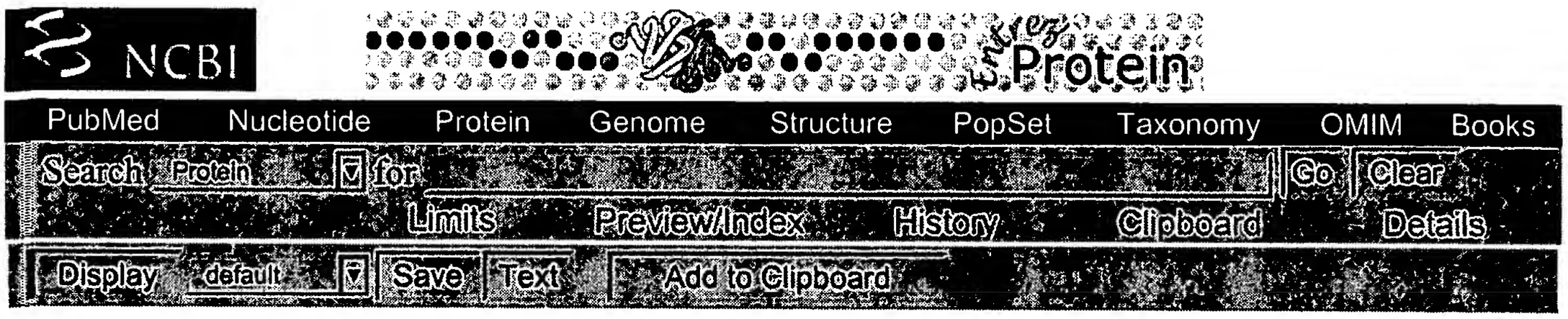
Revised: July 5, 2002.



1: NP_653318. hypothetical prot...[gi:21389499]

BLink, Nucleotide, Related Sequences, Taxonomy, LinkOut

```
LOCUS       MGC34923                  169 aa            linear   PRI 11-JUN-2002
DEFINITION  hypothetical protein MGC34923 [Homo sapiens].
ACCESSION   NP_653318
VERSION     NP_653318.1  GI:21389499
DBSOURCE    REFSEQ: accession NM_144717.1
KEYWORDS    .
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (residues 1 to 169)
  AUTHORS   Strausberg,R.
  TITLE     Homo sapiens hypothetical protein MGC34923 (MGC34923), mRNA
  JOURNAL   Unpublished (2002)
COMMENT     PREDICTED REFSEQ: The mRNA record is supported by experimental
            evidence; however, the coding sequence is predicted. The reference
            sequence was derived from BC027449.1.
FEATURES             Location/Qualifiers
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                     /chromosome="3"
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                     /lab_host="DH10B"
                     /note="Vector: pCMV-SPORT6"
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     CDS             1..169
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      121 ysccpvvvlp dtlkitnspq kliscrreev dacatavmsp eellrawis
//
```

Revised: July 5, 2002.

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Conserved Domain Database

PubMed Nucleotide Protein Structure **CDD** Taxonomy Help?

CD: pfam01108.5, Tissue_fac **PSSM-Id:** 1658 **Source:** Pfam[US], Pfam[UK

Description: Tissue factor.

Taxa: Eutheria **References:** 1 Pubmed Link

Status: Alignment from source **Created:** 13-Jun-2002

Aligned: 5 rows **PSSM:** 293 columns **Representative:** Consensus

Proteins: [Click here for CDART summary of Proteins containing pfam01108]

View Alignment as Hypertext width 60 color at 2.0 bits

Subset Rows up to 10 of the most diverse members

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                    10        20        30        40        50        60
                    ....*....|....*....|....*....|....*....|....*....|....*....|
consensus     1 MATPVRPRVPRPETAVARTLLLGWLLAQVAGAAGTTE--KAYNLTWKSTNFKTILEWEPK 58
gi 135666     1 METPAWPRVPRPETAVARTLLLGWVFAQVAGASGTTNtvAAYNLTWKSTNFKTILEWEPK 60
gi 135668     1 MAPPTRLQVPRPGTAVPYTVLLGWLLAQVARAADTTG--RAYNLTWKSTNFKTILEWEPK 58
gi 401175     1 MATPNGPRVPCPQAAVARALLFGLVLIQGAGVAGTTDvvVAYNITWKSTNFKTILEWEPK 60
gi 135667     1 MAILVRPRL----LAALAPTFLGCLLLQVIAGAGIPE--KAFNLTWISTDFKTILEWQPK 54

                    70        80        90       100       110       120
                    ....*....|....*....|....*....|....*....|....*....|....*....|
consensus    59 PINHVYTVQISTRSGNWKNKCFYTTDTECDLTDEIVKDVTQTYLARVLSYPARN------ 112
gi 135666    61 PVNQVYTVQISTKSGDWKSKCFYTTDTECDLTDEIVKDVKQTYLARVFSYPAGN------ 114
gi 135668    59 SIDHVYTVQISTRLENWKSKCFLTAETECDLTDEVVKDVGQTYMARVLSYPARN------ 112
gi 401175    61 PINHVYTVQISPRLGNWKNKCFYTTNTECDVTDEIVKNVRETYLARVLSYPA-------- 112
gi 135667    55 PTNYTYTVQISDRSRNWKNKCFSTTDTECDLTDEIVKDVTWAYEAKVLSVPRRNsvhgdg 114

                   130       140       150       160       170       180
                    ....*....|....*....|....*....|....*....|....*....|....*....|
consensus   113 DQTTGSGEEPPFTNSPEFTPYLDTNLGQPTIQSFEQVGTKLNVTVQDARTLVRRNGTFLS 172
gi 135666   115 VESTGSAGEPLYENSPEFTPYLETNLGQPTIQSFEQVGTKVNVTVEDERTLVRRNNTFLS 174
gi 135668   113 GNTTGFPEEPPFRNSPEFTPYLDTNLGQPTIQSFEQVGTKLNVTVQDARTLVRRNGTFLS 172
gi 401175   113 -DTSSSTVEPPFTNSPEFTPYLETNLGQPTIQSFEQVGTKLNVTVQDARTLVRANSAFLS 171
gi 135667   115 DQLVIHGEEPPFTNAPKFLPYRDTNLGQPVIQQFEQDGRKLNVVVKDSLTLVRKNGTFLT 174

                   190       200       210       220       230       240
                    ....*....|....*....|....*....|....*....|....*....|....*....|
consensus   173 LRDVFGKDLNYTLYYWKASSTGKKTATTNTNEFLIDVDKGENYCFSVQAVIPSRKVNQKS 232
gi 135666   175 LRDVFGKDLIYTLYYWKSSSSGKKTAKTNTNEFLIDVDKGENYCFSVQAVIPSRTVNRKS 234
gi 135668   173 LRAVFGKDLNYTLYYWRASSTGKKTATTNTNEFLIDVDKGENYCFSVQAVIPSRKRKQRS 232
gi 401175   172 LRDVFGKDLNYTLYYWKASSTGKKKATTNTNGFLIDVDKGENYCFHVQAVILSRRVNQKS 231
gi 135667   175 LRQVFGKDLGYIITYRKGSSTGKKTNITNTNEFSIDVEEGVSYCFFVQAMIFSRKTNQNS 234

                   250       260       270       280       290       300
                    ....*....|....*....|....*....|....*....|....*....|....*....|
consensus   233 PESPTECTSQEKGFLRETFFIIGAVVLVVIIFIIVLSISLHKCRKARAGQSGKENTPLNL 292
gi 135666   235 TDSPVECMGQEKGEFREIFYIIGAVVFVVIILVIILAISLHKCRKAGVGQSWKENSPLNV 294
gi 135668   233 PESLTECTSREQGRAREMFFIIGAVV-VVALLIIVLSVTVYKCRKARAGPSGKESSPLNI 291
gi 401175   232 PESPIKCTSHEKVLSTELFFIIGTVMLVIIIFIVVLSVSLHKCRKVRAERSGKENTPLNA 291
gi 135667   235 PGSSTVCTEQWKSFLGETLIIVGAVVLLATIFIILLSISLCKRRKNRAGQKGK-NTPSRL 293

consensus   293 A 293
gi 135666   295 S 295
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gi 135668	292	A	292
gi 401175	292	A	292
gi 135667	294	A	294

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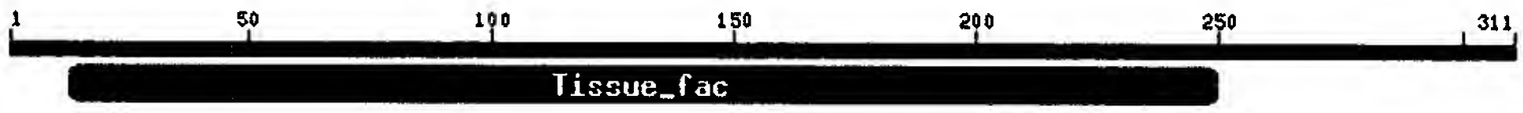
NCBI Conserved Domain Search

RPS-BLAST 2.2.3 [Apr-24-2002]

Query= local sequence:
(311 letters)

Database: oasis_sap.v1.58
4540 PSSMs; 885,521 total columns

Click on boxes for multiple alignments



Show Domain Relatives

PSSMs producing significant alignments:	Score (bits)	E value
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gnl|CDD|1658, pfam01108, Tissue_fac, Tissue factor.

CD-Length = 293 residues, 85.0% aligned
Score = 37.4 bits (86), Expect = 7e-04

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Query:  73   EYESLYTSHIWIPSSWCSLTEGPECDVTDDITATV--PYNLRVRATLGSQTSAWSILKHP  130
Sbjct:  71   RSGN------W--KNKCFYTTDTECDLTDEIVKDVTQTYLARVLSYPARNDQTTGSGEEP  122

Query:  131  FNRNS--------TILTRPGME-IXKXGFHLVIELED----------------LGPQFE  164
Sbjct:  123  PFTNSPEFTPYLDTNLGQPTIQSFEQVGTKLNVTVQDARTLVRRNGTFLSLRDVFGKDLN  182

Query:  165  FLVAYWXREPGAEEHVKMVRSGGIPVHLETMEPGAAYC--VKAQTFVKAIGXYSAFSQTE  222
Sbjct:  183  YTLYYWKASSTGKKTATTNTNE----FLIDVDKGENYCFSVQAVIPSRKVNQKSPESPTE  238

Query:  223  CVXV-QGEAIPLVLALFAFVGFMLILVVV  250
Sbjct:  239  CTSQEKGFLRETFFIIGAVVLVVIIFIIV  267
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NCBI **results of BLAST**

BLASTP 2.2.3 [Apr-24-2002]

Reference:
Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schäffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402.

RID: 1028827051-0733-14680

Query=
(311 letters)

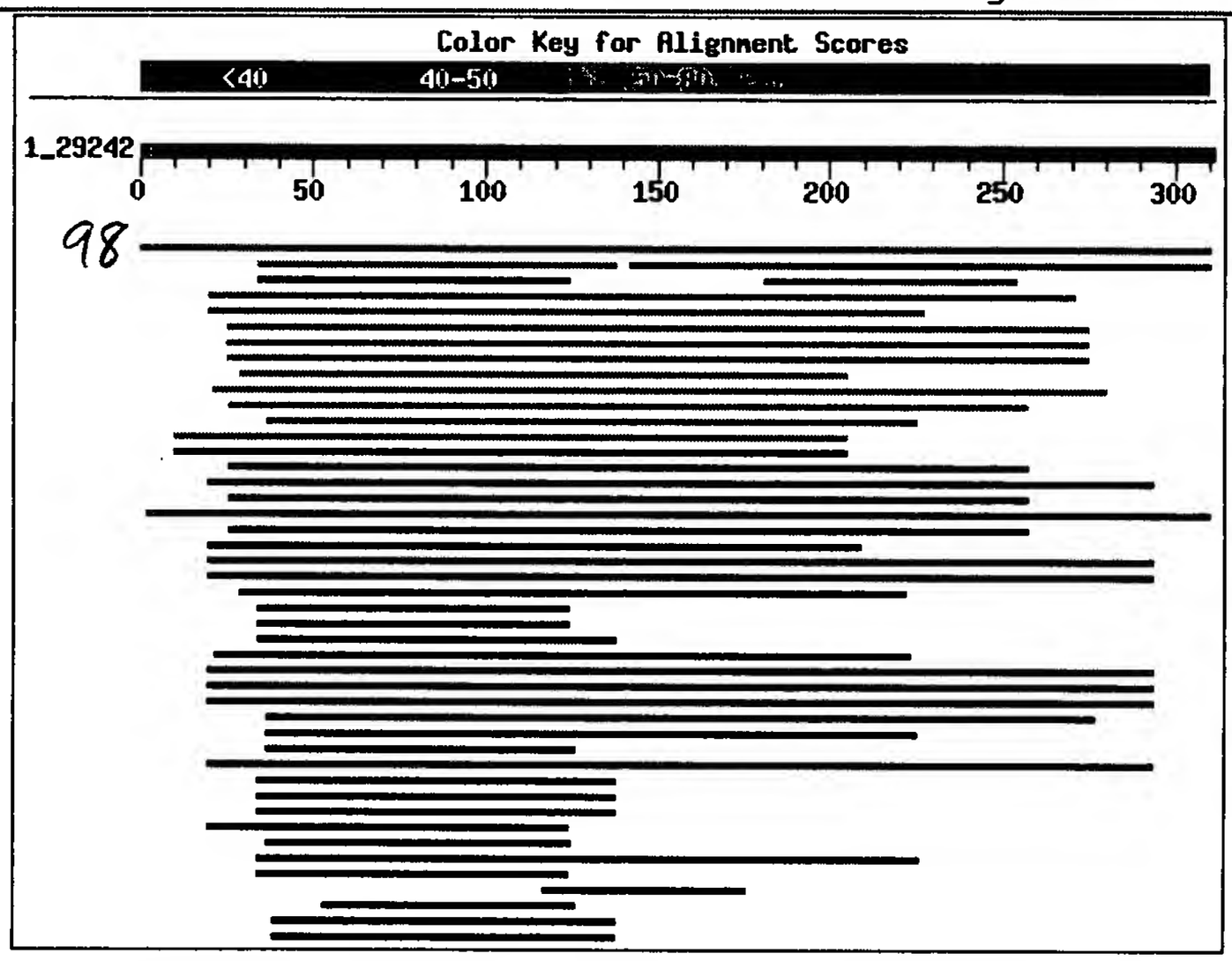
Database: All non-redundant GenBank CDS translations+PDB+SwissProt+PIR+PRF
1,047,264 sequences; 330,262,426 total letters

If you have any problems or questions with the results of this search please refer to the **BLAST FAQs**

Taxonomy reports

Distribution of 50 Blast Hits on the Query Sequence

Mouse-over to show defline and scores. Click to show alignments



Sequences producing significant alignments: Score (bits) E Value

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gi|21389499|ref|NP_653318.1| (NM_144717) hypothetical prote...	323	2e-87	L
gi|20893710|ref|XP_135077.1| (XM_135077) hypothetical prote...	77	2e-13	L
gi|4028135|gb|AAD13669.1| (AF082664) interferon alpha/beta ...	69	1e-10	
gi|4028143|gb|AAD13679.1| (AF082667) interferon alpha/beta ...	61	1e-08	
gi|20560916|ref|XP_114185.1| (XM_114185) interleukin 10 rec...	59	6e-08	
gi|19923113|ref|NP_000619.2| (NM_000628) interleukin 10 rec...	59	6e-08	L
gi|7512371|pir||G01418 cytokine receptor family II, member ...	58	1e-07	
gi|18593097|ref|XP_048563.2| (XM_048563) interferon gamma r...	54	2e-06	
gi|4028139|gb|AAD13671.1| (AF082666) interleukin-10 recepto...	52	1e-05	
gi|7513699|pir||JC6311 interferon receptor-class II cytokin...	51	2e-05	
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gi|463552|gb|AAA16956.1| (U05877) AF-1 [Homo sapiens] >gi|1...	50	3e-05	L
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gi|17646388|gb|AAL40946.1|AF440787_1 (AF440787) interleukin...	49	5e-05	L
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gi|6754302|ref|NP_034638.1| (NM_010508) interferon (alpha a...	48	2e-04	L
gi|20896187|ref|XP_128323.1| (XM_128323) similar to interle...	47	2e-04	L
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gi|2494729|sp|Q28589|INR1_SHEEP INTERFERON-ALPHA/BETA RECEP...	46	4e-04	
gi|6680373|ref|NP_032364.1| (NM_008338) interferon gamma re...	46	5e-04	L
gi|7657691|ref|NP_055247.1| (NM_014432) interleukin 20 rece...	46	6e-04	L
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gi|6680389|ref|NP_032374.1| (NM_008348) interleukin 10 rece...	45	0.001	L
gi|20856437|ref|XP_136952.1| (XM_136952) similar to bA204P2...	44	0.002	L
gi|10835183|ref|NP_000620.1| (NM_000629) interferon (alpha,...	43	0.005	L
gi|16166194|ref|XP_048562.2| (XM_048562) similar to interfe...	43	0.005	L
gi|32672|emb|CAA42992.1| (X60459) interferon alpha/beta rec...	43	0.005	L
gi|4028137|gb|AAD13670.1| (AF082665) interferon alpha/beta ...	42	0.009	
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gi|4504633|ref|NP_001549.1| (NM_001558) interleukin 10 rece...	40	0.036	L
gi|20560751|ref|XP_006447.7| (XM_006447) similar to Interle...	40	0.036	L
gi|11991877|gb|AAG42376.1|AF296666_1 (AF296666) type I inte...	40	0.044	
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gi|20896935|ref|XP_139651.1| (XM_139651) similar to INTERFE...	35	0.80	L
gi|18547428|ref|XP_089078.1| (XM_089078) similar to interle...	35	0.85	L
gi|15602147|ref|NP_245219.1| (NC_002663) unknown [Pasteurel...	33	3.6	
gi|2129405|pir||S53867 DNA (cytosine)-methyltransferase (EC...	33	4.6	
gi|3980170|emb|CAA37597.1| (X53521) brain tissue factor [Or...	32	6.8	
gi|3212253|pdb|1A21|B Chain B, Tissue Factor (Tf) From Rabb...	32	7.0	

Alignments

>gi|20536050|ref|XP_087367.2| (XM_087367) similar to interleukin 10 receptor, beta receptor family II, member 4; human transmembrane receptor protein; cytokine receptor [Homo sapiens]
Length = 311

Score = 597 bits (1539), Expect = e-170
Identities = 306/311 (98%), Positives = 306/311 (98%)

```
Query: 1   MQTFTMVLEEIWTSLFMWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAP 60
           MQTFTMVLEEIWTSLFMWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAP
Sbjct: 1   MQTFTMVLEEIWTSLFMWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAP 60
```

```
Query: 61   GETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQ 120
            GETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQ
Sbjct: 61   GETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQ 120

Query: 121 TSAWSILKHPFNRNSTILTRPGMEIXKXGFHLVIELEDLGPQFEFLVAYWXREPGAEEHV 180
            TSAWSILKHPFNRNSTILTRPGMEI K GFHLVIELEDLGPQFEFLVAYW REPGAEEHV
Sbjct: 121 TSAWSILKHPFNRNSTILTRPGMEITKDGFHLVIELEDLGPQFEFLVAYWRREPGAEEHV 180

Query: 181 KMVRSGGIPVHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTECVXVQGEAIPLVLALFAF 240
            KMVRSGGIPVHLETMEPGAAYCVKAQTFVKAIG YSAFSQTECV VQGEAIPLVLALFAF
Sbjct: 181 KMVRSGGIPVHLETMEPGAAYCVKAQTFVKAIGRYSAFSQTECVEVQGEAIPLVLALFAF 240

Query: 241 VGFMLILVVVPLFVWKMGRLLQYSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVM 300
            VGFMLILVVVPLFVWKMGRLLQYSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVM
Sbjct: 241 VGFMLILVVVPLFVWKMGRLLQYSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVM 300

Query: 301 SPEELLRAWIS 311
            SPEELLRAWIS
Sbjct: 301 SPEELLRAWIS 311
```

>gi|21389499|ref|NP_653318.1| (NM_144717) hypothetical protein MGC34923 [Homo sap
gi|20072749|gb|AAH27449.1| (BC027449) similar to interferon alpha/beta receptor
sapiens]
Length = 169

Score = 323 bits (827), Expect = 2e-87
Identities = 164/169 (97%), Positives = 164/169 (97%)

```
Query: 143 MEIXKXGFHLVIELEDLGPQFEFLVAYWXREPGAEEHVKMVRSGGIPVHLETMEPGAAYC 202
            MEI K GFHLVIELEDLGPQFEFLVAYW REPGAEEHVKMVRSGGIPVHLETMEPGAAYC
Sbjct: 1   MEITKDGFHLVIELEDLGPQFEFLVAYWRREPGAEEHVKMVRSGGIPVHLETMEPGAAYC 60

Query: 203 VKAQTFVKAIGXYSAFSQTECVXVQGEAIPLVLALFAFVGFMLILVVVPLFVWKMGRLLQ 262
            VKAQTFVKAIG YSAFSQTECV VQGEAIPLVLALFAFVGFMLILVVVPLFVWKMGRLLQ
Sbjct: 61  VKAQTFVKAIGRYSAFSQTECVEVQGEAIPLVLALFAFVGFMLILVVVPLFVWKMGRLLQ 120

Query: 263 YSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVMSPEELLRAWIS 311
            YSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVMSPEELLRAWIS
Sbjct: 121 YSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVMSPEELLRAWIS 169
```

>gi|20893710|ref|XP_135077.1| (XM_135077) hypothetical protein XP_135077 [Mus mus
Length = 112

Score = 77.4 bits (189), Expect = 2e-13
Identities = 44/74 (59%), Positives = 48/74 (64%), Gaps = 7/74 (9%)

```
Query: 182 MVRSGGIPVHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTECVXVQGEAIPLVLALFAFV 241
            MVRSG IPVHLETMEPGA YCVKAQ  VKAIG +SAFSQ  CV +QG+   LV
Sbjct: 1   MVRSGDIPVHLETMEPGAMYCVKAQALVKAIGRHSAFSQPTCVEMQGKDNLLVPG----- 55

Query: 242 GFMLILVVVPLFVW 255
               L L  +PL  W
Sbjct: 56  --SLHLAALPLHAW 67
```

>gi|4028135|gb|AAD13669.1| (AF082664) interferon alpha/beta receptor 1 [Gallus gal
Length = 569

Score = 68.6 bits (166), Expect = 1e-10
Identities = 73/273 (26%), Positives = 117/273 (42%), Gaps = 25/273 (9%)

```
Query: 21  YALIPCL-LTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEY-QGEYESLY 78
            ++ I C+  T +V  L  P N+ V + NMK  L+W       E V Y+V+Y  G  ++LY
Sbjct: 222 FSPIHCIKTTRKVNDLLCPTNVRVFALNMKFYLLWDNHY--NEHVTYTVQYLTGYLKNLY 279
```

```
Query: 79  T--SHIWIPSSWCSLTEGPECDVTDDITAT-VPYNLRVRATLGSQTSAWS--ILKHPFNR 133
              S  W   S C      +C+++  I  T   Y  RV+A      S  S  +   P
Sbjct: 280 DDYSSKWQKVSGCENITSMKCNLSSVIKPTSASYYFRVQAMNEYSKSCLSKDVEVDPPVT 339

Query: 134 NSTILTRPGMEIXKXGFHLVIE---------LEDLGPQFEFLVAYWXREPGAEEHVKMVR 184
            N        ++I     H+ I           + DL   F + + YW      EE VKM
Sbjct: 340 NEIGPPDVKVDISDVLLHIKITPPGGPGNKIMSDL-YDFSYQILYWKNSSDNEEEVKMKE 398

Query: 185 SGGIPVHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTECVXVQ-GEAIPLVLALFAFVGF 243
            +      +  + P   YCVK Q F +A    S FS+ EC+    G+ +PL++ L  F G
Sbjct: 399 TKQTIATVSDLAPSTLYCVKVQAFSEAYNKSSDFSREECIGTAGGKHLPLII-LATFAGA 457

Query: 244 MLILVVVP----LFVWKMGRLLQYSCCPVVVLP 272
            + ++++V      F++++   ++Y   P    P
Sbjct: 458 LTVVLIVASLVIFFLYQVYNKIKYMFFPSCQTP 490
```

Score = 47.4 bits (111), Expect = 2e-04
Identities = 53/206 (25%), Positives = 82/206 (39%), Gaps = 25/206 (12%)

```
Query: 35  LPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTSHI-WIPSSWCSLTE 93
           L +PQ++ V + N    LMW+     G  V +S +YQ  ++ L TS   W   S C
Sbjct: 32  LKSPQDIQVYAVNTNFTLMWN-YTGDGTNVTFSAQYQC-FDDLQTSEPEWKELSGCQNVS 89

Query: 94  GPECDVTDDITATV-PYNLRVRATLGSQTSAWSILKHPFNRNSTILTRPGMEIXKXGFHL 152
             ECD +  ITA    +++R+RA      S WS +           +  P  EI     +
Sbjct: 90  HTECDFSSAITAYYDTHHIRIRAERREAKSPWSSIFEMIPYEIAQIGPP--EIALQSING 147

Query: 153 VIELEDLGPQ-----------FEFLVAYWXREPGAEEHVKMVRSGGIPVH-LETMEPG 198
             I++    P+               F++ V  W      E+    VRS  +P+  +  + P
Sbjct: 148 AIKINISPPEANQVRKMWLISVFFKYNVVIWDNSSNVEK----VRS-ILPIDVINDLAPE 202

Query: 199 AAYCVKAQTFVKAIGXYSAFSQTECV 224
             YC+K Q  V       FS   C+
Sbjct: 203 TTYCLKVQATVPLEDKGGLFSPIHCI 228
```

>gi|4028143|gb|AAD13679.1| (AF082667) interferon alpha/beta receptor 1 [Gallus gal
Length = 442

Score = 61.2 bits (147), Expect = 1e-08
Identities = 63/224 (28%), Positives = 92/224 (40%), Gaps = 19/224 (8%)

```
Query: 21  YALIPCL-LTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEY-QGEYESLY 78
           ++ I C+  T +V  L  P N+ V + NMK  L+W       E V Y+V+Y  G  ++LY
Sbjct: 222 FSPIHCIKTTRKVNDLLCPTNVRVFALNMKFYLLWDNHY--NEHVTYTVQYLTGYLKNLY 279
```


```
Query: 79  T--SHIWIPSSWCSLTEGPECDVTDDITAT-VPYNLRVRATLGSQTSAWS--ILKHPFNR 133
              S  W   S C      +C+++  I  T   Y  RV+A      S  S  +   P
Sbjct: 280 DDYSSKWQKVSGCENITSMKCNLSSVIKPTSASYYFRVQAMNEYSKSCLSKDVEVDPPVT 339

Query: 134 NSTILTRPGMEIXKXGFHLVIE---------LEDLGPQFEFLVAYWXREPGAEEHVKMVR 184
            N        ++I     H+ I           + DL   F + + YW      EE VKM
Sbjct: 340 NEIGPPDVKVDISDVLLHIKITPPGGPGNKIMSDL-YDFSYQILYWKNSSDNEEEVKMKE 398
```


```
Query: 185 SGGIPVHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTECVXVQG 228
           +      +  + P   YCVK Q F +A    S FS+ EC+   G
Sbjct: 399 TKQTIATVSDLAPSTLYCVKVQAFSEAYNKSSDFSREECIGTAG 442
```

Score = 47.8 bits (112), Expect = 2e-04
Identities = 53/206 (25%), Positives = 82/206 (39%), Gaps = 25/206 (12%)

```
Query: 35  LPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTSHI-WIPSSWCSLTE 93
           L +PQ++ V + N    LMW+     G  V +S +YQ  ++ L TS   W   S C
Sbjct: 32  LKSPQDIQVYAVNTNFTLMWN-YTGDGTNVTFSAQYQC-FDDLQTSEPEWKELSGCQNVS 89
```

```
Query: 94   GPECDVTDDITATV-PYNLRVRATLGSQTSAWSILKHPFNRNSTILTRPGMEIXKXGFHL 152
              ECD +  ITA    +++R+RA      S WS +          +  P  EI     +
Sbjct: 90   HTECDFSSAITAYYDTHHIRIRAERREAKSPWSSIFEMIPYEIAQIGPP--EIALQSING 147

Query: 153 VIELEDLGPQ-------------FEFLVAYWXREPGAEEHVKMVRSGGIPVH-LETMEPG 198
             I++    P+               F++ V  W      E+    VRS  +P+  +  + P
Sbjct: 148 AIKINISPPEANQVRKMWLISVFFKYNVVIWDNSSNVEK----VRS-ILPIDVINDLAPE 202

Query: 199 AAYCVKAQTFVKAIGXYSAFSQTECV 224
              YC+K Q  V         FS   C+
Sbjct: 203 TTYCLKVQATVPLEDKEGLFSPIHCI 228

>gi|20560916|ref|XP_114185.1|   (XM_114185) interleukin 10 receptor, beta [Homo sapi
 gi|12804903|gb|AAH01903.1|AAH01903   (BC001903) Similar to interleukin 10 receptor,
          Length = 325

 Score = 59.3 bits (142), Expect = 6e-08
 Identities = 69/272 (25%), Positives = 116/272 (42%), Gaps = 37/272 (13%)

Query: 26   CLLTDEVAILPAPQNLSVLSTNMKHLLMW-SPVIAPGETVYYSVEYQGEYESLYTSHIWI 84
             CLL    + ++P  P+N+  + S  N  K++L  W SP   A  G      ++  +Y S       I
Sbjct: 12   CLLVSALGMVPPPENVRMNSVNFKNILQWESPAFAKG-----NLTFTAQYLSYR-----I 61

Query: 85   PSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAW-SILKHPFNRNSTILTRPGM 143
                C  T   ECD +  ++    + LRVRA    + S W +I   P   + TI+  PGM
Sbjct: 62   FQDKCMNTTLTECDFS-SLSKYGDHTLRVRAEFADEHSDWVNITFCPV--DDTIIGPPGM 118

Query: 144  --EIXKXGFHLVIELEDLGPQFE-------------FLVAYWXREPGAEEHVKMVRSGGIP 189
               E+     H+       +  ++E                + V YW   + G  +E   ++
Sbjct: 119  QVEVLADSLHMRFLAPKIENEYETWTMKNVYNSWTYNVQYW--KNGTDEKFQITPQYDFE 176

Query: 190  VHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTEC-VXVQGEAIP--LVLALFAFVGFMLI 246
             V L  +EP   YCV+ + F+          +S+  C       E +P  +V   +  FM+
Sbjct: 177  V-LRNLEPWTTYCVQVRGFLPDRNKAGEWSEPVCEQTTHDETVPSWMVAVILMASVFMVC 235

Query: 247  LVVVPLF--VWKMGRLLQYSCCPVVVLPDTLK 276
              L ++   F  +W + +  +Y+  P    LP  LK
Sbjct: 236  LALLGCFALLWCVYKKTKYAFSPRNSLPQHLK 267

>gi|19923113|ref|NP_000619.2|  L (NM_000628) interleukin 10 receptor, beta; cytokine
          II, member 4; human transmembrane receptor protein;
          cytokine receptor [Homo sapiens]
 gi|729209|sp|Q08334|I10S_HUMAN   Interleukin-10 receptor beta chain precursor (IL-1
          (Cytokine receptor class-II CRF2-4)
 gi|627419|pir||A47003   cytokine receptor family class II protein CRF2-4 precursor
 gi|393379|emb|CAA78933.1|  L (Z17227) transmembrane receptor precusor [Homo sapiens
          Length = 325

 Score = 59.3 bits (142), Expect = 6e-08
 Identities = 69/272 (25%), Positives = 116/272 (42%), Gaps = 37/272 (13%)

Query: 26   CLLTDEVAILPAPQNLSVLSTNMKHLLMW-SPVIAPGETVYYSVEYQGEYESLYTSHIWI 84
             CLL    + ++P  P+N+  + S  N  K++L  W SP   A  G      ++  +Y S       I
Sbjct: 12   CLLVSALGMVPPPENVRMNSVNFKNILQWESPAFAKG-----NLTFTAQYLSYR-----I 61

Query: 85   PSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAW-SILKHPFNRNSTILTRPGM 143
                C  T   ECD +  ++    + LRVRA    + S W +I   P   + TI+  PGM
Sbjct: 62   FQDKCMNTTLTECDFS-SLSKYGDHTLRVRAEFADEHSDWVNITFCPV--DDTIIGPPGM 118

Query: 144  --EIXKXGFHLVIELEDLGPQFE-------------FLVAYWXREPGAEEHVKMVRSGGIP 189
               E+     H+       +  ++E                + V YW   + G  +E   ++
Sbjct: 119  QVEVLADSLHMRFLAPKIENEYETWTMKNVYNSWTYNVQYW--KNGTDEKFQITPQYDFE 176

Query: 190  VHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTEC-VXVQGEAIP--LVLALFAFVGFMLI 246
             V L  +EP   YCV+ + F+          +S+  C       E +P  +V   +  FM+
Sbjct: 177  V-LRNLEPWTTYCVQVRGFLPDRNKAGEWSEPVCEQTTHDETVPSWMVAVILMASVFMVC 235

Query: 247  LVVVPLF--VWKMGRLLQYSCCPVVVLPDTLK 276
              L ++   F  +W + +  +Y+  P    LP  LK
Sbjct: 236  LALLGCFALLWCVYKKTKYAFSPRNSLPQHLK 267
```

```
                V L  +EP   YCV+ + F+        +S+  C      E +P  +V  +     FM+
Sbjct: 177 V-LRNLEPWTTYCVQVRGFLPDRNKAGEWSEPVCEQTTHDETVPSWMVAVILMASVFMVC 235

Query: 247 LVVVPLF--VWKMGRLLQYSCCPVVVLPDTLK 276
            L ++  F  +W + +  +Y+  P   LP  LK
Sbjct: 236 LALLGCFSLLWCVYKKTKYAFSPRNSLPQHLK 267

>gi|7512371|pir||G01418   cytokine receptor family II, member 4 - human
 gi|571296|gb|AAA86872.1|  L (U08988) CRFB4 [Homo sapiens]
          Length = 273

 Score = 58.2 bits (139), Expect = 1e-07
 Identities = 69/272 (25%), Positives = 116/272 (42%), Gaps = 37/272 (13%)

Query: 26  CLLTDEVAILPAPQNLSVLSTNMKHLLMW-SPVIAPGETVYYSVEYQGEYESLYTSHIWI 84
            CLL   + ++P P+N+ + S N K++L W SP  A G     ++ +  +Y S       I
Sbjct: 12  CLLVSALGMVPPPENVRMNSVNFKNILQWESPAFAKG-----NLTFTAQYLSYR-----I 61

Query: 85  PSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAW-SILKHPFNRNSTILTRPGM 143
                C  T   ECD + ++     + LRVRA    + S W +I   P   + TI+  PGM
Sbjct: 62  FQDKCMNTTLTECDFS-SLSKYGDHTLRVRAEFADEHSDWVNITFCPV--DDTIIGPPGM 118

Query: 144 --EIXKXGFHLVIELEDLGPQFE------------FLVAYWXREPGAEEHVKMVRSGGIP 189
              E+     H+      +  ++E            + V YW  + G +E  ++
Sbjct: 119 QVEVLDDSLHMRFLAPKIENEYETWTMKNVYNSWTYNVQYW--KNGTDEKFQITPQYDFE 176

Query: 190 VHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTEC-VXVQGEAIP--LVLALFAFVGFMLI 246
            V L  +EP   YCV+ + F+        +S+  C      E +P  +V  +     FM+
Sbjct: 177 V-LRNLEPWTTYCVQVRGFLPDRNKAGEWSEPVCEQTTHDETVPSWMVAVILMASVFMVC 235

Query: 247 LVVVPLF--VWKMGRLLQYSCCPVVVLPDTLK 276
            L ++  F  +W + +  +Y+  P   LP  LK
Sbjct: 236 LALLGCFSLLWCVYKKTKYAFSPRNSLPQHLK 267

>gi|18593097|ref|XP_048563.2|   (XM_048563) interferon gamma receptor accessory fact
           sapiens]
          Length = 356

 Score = 53.9 bits (128), Expect = 2e-06
 Identities = 56/193 (29%), Positives = 85/193 (44%), Gaps = 20/193 (10%)

Query: 30  DEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGET--VYYSVEYQGEYESLYTSHIWIPSS 87
            D ++ LPAPQ+  +   N + +L W PV     T  V Y V+++      +T+ I
Sbjct: 44  DPLSQLPAPQHPKIRLYNAEQVLSWEPVALSNSTRPVVYQVQFKYTDSKWFTADIMSIGV 103

Query: 88  WCSLTEGPECDVT-DDITATVPYN----LRVRATLGSQTSAWSILK-HPFNRNSTILTRP 141
             C+     ECD T    +A  P +    LR+RA LG+  SAW  +      RN T+
Sbjct: 104 NCTQITATECDFTAASPSAGFPMDFNVTLRLRAELGALHSAWVTMPWFQHYRNVTVGPPE 163

Query: 142 GMEIXKXGFHLVIELE---DLGPQ----FEFLVAYWXREPGAEEHVK-MVRSGGIPVHLE 193
             +E+      L+I      D+       F + V YW  E G  + VK   RS  I   L+
Sbjct: 164 NIEVTPGEGSLIIRFSSPFDIADTSTAFFCYYVHYW--EKGGIQQVKGPFRSNSIS--LD 219

Query: 194 TMEPGAAYCVKAQ 206
             ++P   YC++ Q
Sbjct: 220 NLKPSRVYCLQVQ 232

>gi|4028139|gb|AAD13671.1|   (AF082666) interleukin-10 receptor 2 [Gallus gallus]
 gi|4028142|gb|AAD13678.1|   (AF082667) interleukin-10 receptor 2 [Gallus gallus]
          Length = 341

 Score = 51.6 bits (122), Expect = 1e-05
 Identities = 59/279 (21%), Positives = 115/279 (41%), Gaps = 29/279 (10%)

Query: 22  ALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTSH 81
```

```
            AL  CLL     I+P P+N  + S N + +L+W P       + Y+V+ +  +     ++
Sbjct: 8    ALWGCLLLCVSGIVPKPRNARISSVNFRSVLLWDPPGVRKGNLSYTVQAKSIFPKQNFNN 67

Query: 82   IWIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSILKHPFNRNSTILTRP 141
            +   ++  ++T   ECDV+  ++    Y LRVR     + S W++++       T++  P
Sbjct: 68   V---TTNLNVT---ECDVS-SLSVYGAYVLRVRTEWEDEHSDWAVVRFK-PMADTVIGPP 119

Query: 142  GMEIXKXGFHLVIELEDLGPQFE--------------FLVAYWXREPGAEEHVKMVRSGG 187
             + +      L ++         E                + + YW +  G+ + V  + +
Sbjct: 120  SVNVKSESGTLHVDFTGPAADREHDKWSLKQYYGSWIYRILYWKK--GSNKKVIHIDTKH 177

Query: 188  IPVHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTECVXVQGEAI-PLVLALFAFVGFML- 245
                L  +EP   YC++ Q  +          SQ  C       + P+ + +   +G ML
Sbjct: 178  NSEILSQLEPWTIYCIQVQGVIPEWNKTGERSQELCEQTTHNGVTPVWIVVTVLLGSMLA 237

Query: 246  ILVVVPL---FVWKMGRLLQYSCCPVVVLPDTLKITNSP 281
                +++ VP+     W + R  ++   P  + P  LK   SP
Sbjct: 238  VIISVPVCFFAFWYLYRFTKHVFFPSYIFPQHLKEFFSP 276
```

>gi|7513699|pir||JC6311 interferon receptor-class II cytokine receptor - mouse
Length = 349

Score = 51.2 bits (121), Expect = 2e-05
Identities = 61/249 (24%), Positives = 103/249 (40%), Gaps = 38/249 (15%)

```
Query: 27   LLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPS 86
             LL   + ++P P+ + + S N K++L W     P   + ++ +Y+  Y S +  H
Sbjct: 13   LLVPALGMIPPPEKVRMNSVNFKNILQWEVPAFPKTNLTFTAQYE-SYRS-FQDH----- 65

Query: 87   SWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAW-SILKHPFNRNSTILTRPGMEI 145
               C  T   +CD +  ++    Y +RVRA L  + S W ++   P     TI+  P M+I
Sbjct: 66   --CKRTASTQCDFS-HLSKYGDYTVRVRAELADEHSEWVNVTFCPV--EDTIIGPPEMQI 120

Query: 146  XKXGFHLVIELEDLGPQFE---------------FLVAYWXREPGAEEHVKMVRSGGIP 189
                  L  EL    PQ E                 + V YW  + G   E  ++V
Sbjct: 121  ESLAESL--ELRFSAPQIENEPETWTLKNIYDSWAYRVQYW--KNGTNEKFQVVSPYDSE 176

Query: 190  VHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTECVXVQGEAIPLVLALFAFVGFMLILVV 249
             V L  +EP   YC++ Q F+        +S+  C     + I          V  +LI+ V
Sbjct: 177  V-LRNLEPWTTYCIQVQGFLLDQNRTGEWSEPICERTGNDEITPSW----IVAIILIVSV 231

Query: 250  VPLFVWKMG 258
             P+F+W+ G
Sbjct: 232  APVFLWRKG 240
```

>gi|17105372|ref|NP_476541.1| (NM_057193) interleukin 10 receptor, alpha [Rattus
gi|12330005|emb|CAC24567.1| (AJ305049) interleukin-10 receptor, alpha chain [Rat
Length = 569

Score = 50.8 bits (120), Expect = 2e-05
Identities = 33/108 (30%), Positives = 50/108 (45%), Gaps = 8/108 (7%)

```
Query: 35   LPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEG 94
             LP+P ++   +   +H+L W  +    E+ YY V  +       Y + IW     CS  +
Sbjct: 26   LPSPSSVWFEARFFQHILRWMSIPNQSESTYYEVALKK-----YGTSIWKDIHICSKAQT 80

Query: 95   PECDVTD---DITATVPYNLRVRATLGSQTSAWSILKHPFNRNSTILT 139
               CD+T    D+  +  Y  RVRA    SQ S W+I   P+  + ILT
Sbjct: 81   LSCDLTTSTLDLYHSSGYRARVRAVDNSQYSNWTITETRFTVDEVILT 128
```

>gi|15212826|gb|AAK85714.1| (AY040566) interleukin 22-binding protein CRF2-10 [Ho
gi|15419023|gb|AAK91775.1| (AY044429) class II cytokine receptor [Homo sapiens]
gi|16304591|emb|CAC85634.1| (AJ313161) soluble cytokine class II receptor, short
sapiens]

gi|17974197|emb|CAC83097.1| (AJ297262) interleukin-22 binding protein [Homo sapi
Length = 231

Score = 50.8 bits (120), Expect = 2e-05
Identities = 49/205 (23%), Positives = 79/205 (37%), Gaps = 21/205 (10%)

```
Query: 38  PQNLSVLSTNMKHLLMWSPVIA-PGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPE 96
           PQ +   S N  ++L W P  A  G +  Y V+Y+     +Y    W     C  T+
Sbjct: 31  PQRVQFQSRNFHNILQWQPGRALTGNSSVYFVQYK-----IYGQRQWKNKEDCWGTQELS 85

Query: 97  CDVTDDIT-ATVPYNLRVRATLGSQTSAWSILKHPFNRNSTILTRPGMEIXKXGFHLVIE 155
           CD+T + +    PY  RVRA      S WS+          T +  P M I +    L++
Sbjct: 86  CDLTSETSDIQEPYYGRVRAASAGSYSEWSMTPRFTPWWETKIDPPVMNITQVNGSLLVI 145

Query: 156 LE--------------DLGPQFEFLVAYWXREPGAEEHVKMVRSGGIPVHLETMEPGAAY 201
           L                +   +E L   +      E+  K+        V  +E + P ++Y
Sbjct: 146 LHAPNLPYRYQKEKNVSIEDYYELLYRVFIINNSLEKEQKVYEGAHRAVEIEALTPHSSY 205

Query: 202 CVKAQTFVKAIGXYSAFSQTECVXV 226
           CV A+ +    +   S  S+  CV +
Sbjct: 206 CVVAEIYQPMLDRRSQRSEERCVEI 230
```

>gi|463552|gb|AAA16956.1| (U05877) AF-1 [Homo sapiens]
gi|13177682|gb|AAH03624.1|AAH03624 (BC003624) interferon gamma receptor 2 (inter
1) [Homo sapiens]
Length = 337

Score = 50.1 bits (118), Expect = 3e-05
Identities = 59/212 (27%), Positives = 92/212 (42%), Gaps = 20/212 (9%)

```
Query: 11  IWTSLFMWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGET--VYYSV 68
           +W+ L +   +A       D ++ LPAPQ+  +   N + +L W PV     T  V Y V
Sbjct: 6   LWSLLLLLGVFAAAAAPPDPLSQLPAPQHPKIRLYNAEQVLSWEPVALSNSTRPVVYQV 65

Query: 69  EYQGEYESLYTSHIWIPSSWCSLTEGPECDVT-DDITATVPYN----LRVRATLGSQTSA 123
           +++      +T+ I      C+     ECD T    +A  P +    LR+RA LG+  SA
Sbjct: 66  QFKYTDSKWFTADIMSIGVNCTQITATECDFTAASPSAGFPMDFNVTLRLRAELGALHSA 125

Query: 124 WSILK-HPFNRNSTILTRPGMEIXKXGFHLVIELE---DLGPQ----FEFLVAYWXREPG 175
           W  +      RN T+     +E+      L+I      D+       F + V YW  E G
Sbjct: 126 WVTMPWFQHYRNVTVGPPENIEVTPGEGSLIIRFSSPFDIADTSTAFFCYYVHYW--EKG 183

Query: 176 AEEHVK-MVRSGGIPVHLETMEPGAAYCVKAQ 206
             + VK    RS   I    L+ ++P    YC++ Q
Sbjct: 184 IQQVKGPFRSNSIS--LDNLKPSRVYCLQVQ 213
```

>gi|5031783|ref|NP_005525.1| (NM_005534) interferon gamma receptor 2 (interferon
transducer 1); interferon gamma receptor accessory
factor-1; interferon-gamma receptor beta chain precursor
[Homo sapiens]
gi|585319|sp|P38484|INGS_HUMAN Interferon-gamma receptor beta chain precursor (In
receptor accessory factor-1) (AF-1) (Interferon-gamma
transducer-1)
gi|2135504|pir||I38500 interferon gamma receptor accessory factor-1 precursor - h
gi|463550|gb|AAA16955.1| (U05875) AF-1 [Homo sapiens]
Length = 337

Score = 49.7 bits (117), Expect = 4e-05
Identities = 59/212 (27%), Positives = 92/212 (42%), Gaps = 20/212 (9%)

```
Query: 11  IWTSLFMWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGET--VYYSV 68
           +W+ L +   +A       D ++ LPAPQ+  +   N + +L W PV     T  V Y V
Sbjct: 6   LWSLLLLLGVFAAAAAPPDPLSQLPAPQHPKIRLYNAEQVLSWEPVALSNSTRPVVYRV 65

Query: 69  EYQGEYESLYTSHIWIPSSWCSLTEGPECDVT-DDITATVPYN----LRVRATLGSQTSA 123
```

```
            +++       +T+ I       C+      ECD T    +A  P +    LR+RA LG+  SA
Sbjct: 66   QFKYTDSKWFTADIMSIGVNCTQITATECDFTAASPSAGFPMDFNVTLRLRAELGALHSA 125

Query: 124 WSILK-HPFNRNSTILTRPGMEIXKXGFHLVIELE---DLGPQ----FEFLVAYWXREPG 175
            W  +      RN T+     +E+      L+I      D+        F + V YW  E G
Sbjct: 126 WVTMPWFQHYRNVTVGPPENIEVTPGEGSLIIRFSSPFDIADTSTAFFCYYVHYW--EKG 183

Query: 176 AEEHVK-MVRSGGIPVHLETMEPGAAYCVKAQ 206
             + VK   RS  I   L+ ++P   YC++ Q
Sbjct: 184 GIQQVKGPFRSNSIS--LDNLKPSRVYCLQVQ 213

>gi|6680391|ref|NP_032375.1|     (NM_008349) interleukin 10 receptor, beta [Mus muscu
 gi|10720037|sp|Q61190|I10S_MOUSE  Interleukin-10 receptor beta chain precursor (IL
           (Cytokine receptor class-II CRF2-4)
 gi|1305489|gb|AAC53062.1|     (U53696) class II cytokine receptor 4 [Mus musculus].
          Length = 349

 Score = 49.7 bits (117), Expect = 5e-05
 Identities = 57/247 (23%), Positives = 104/247 (42%), Gaps = 34/247 (13%)

Query: 27  LLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPS 86
           LL   + ++P P+ + + S N K++L W     P   + ++ +Y+  Y S +  H
Sbjct: 13  LLVPALGMIPPPEKVRMNSVNFKNILQWEVPAFPKTNLTFTAQYE-SYRS-FQDH----- 65

Query: 87  SWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAW-SILKHPFNRNSTILTRPGMEI 145
             C  T   +CD +  ++    Y +RVRA L  + S W ++   P     TI+  P M+I
Sbjct: 66  --CKRTASTQCDFS-HLSKYGDYTVRVRAELADEHSEWVNVTFCPV--EDTIIGPPEMQI 120

Query: 146 XKXGFHLVIE-------------LEDLGPQFEFLVAYWXREPGAEEHVKMVRSGGIPVH 191
              L +                 L+++   + + V YW  + G  E  ++V      V
Sbjct: 121 ESLAESLHLRFSAPQIENEPETWTLKNIYDSWAYRVQYW--KNGTNEKFQVVSPYDSEV- 177

Query: 192 LETMEPGAAYCVKAQTFVKAIGXYSAFSQTECVXVQGEAIPLVLALFAFVGFMLILVVVP 251
           L  +EP   YC++ Q F+        +S+  C     + I          V  +LI+ V+
Sbjct: 178 LRNLEPWTTYCIQVQGFLLDQNRTGEWSEPICERTGNDEITPSW----IVAIILIVSVLV 233

Query: 252 LFVWKMG 258
           +F++ +G
Sbjct: 234 VFLFLLG 240

>gi|17646388|gb|AAL40946.1|AF440787_1     (AF440787) interleukin 10 receptor 2 precur
          Length = 351

 Score = 49.3 bits (116), Expect = 5e-05
 Identities = 57/247 (23%), Positives = 104/247 (42%), Gaps = 34/247 (13%)

Query: 27  LLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPS 86
           LL   + ++P P+ + + S N K++L W     P   + ++ +Y+  Y S +  H
Sbjct: 15  LLVPALGMIPPPEKVRMNSVNFKNILQWEVPAFPKTNLTFTAQYE-SYRS-FQDH----- 67

Query: 87  SWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAW-SILKHPFNRNSTILTRPGMEI 145
             C  T   +CD +  ++    Y +RVRA L  + S W ++   P     TI+  P M+I
Sbjct: 68  --CKRTASTQCDFS-HLSKYGDYTVRVRAELADEHSEWVNVTFCPV--EDTIIGPPEMQI 122

Query: 146 XKXGFHLVIE-------------LEDLGPQFEFLVAYWXREPGAEEHVKMVRSGGIPVH 191
              L +                 L+++   + + V YW  + G  E  ++V      V
Sbjct: 123 ESLAESLHLRFSAPQIENEPETWTLKNIYDSWAYRVQYW--KNGTNEKFQVVSPYDSEV- 179

Query: 192 LETMEPGAAYCVKAQTFVKAIGXYSAFSQTECVXVQGEAIPLVLALFAFVGFMLILVVVP 251
           L  +EP   YC++ Q F+        +S+  C     + I          V  +LI+ V+
Sbjct: 180 LRNLEPWTTYCIQVQGFLLDQNRTGEWSEPICERTGNDEITPSW----IVAIILIVSVLV 235

Query: 252 LFVWKMG 258
           +F++ +G
Sbjct: 236 VFLFLLG 242
```

```
>gi|462415|sp|Q04790|INR1_BOVIN   INTERFERON-ALPHA/BETA RECEPTOR ALPHA CHAIN PRECURS
              (IFN-ALPHA-REC)
 gi|346520|pir||S27387   interferon alpha receptor type 1 precursor - bovine
 gi|432|emb|CAA48484.1|   (X68443) interferon receptor type 1 [Bos taurus]
          Length = 560

 Score = 49.3 bits (116), Expect = 6e-05
 Identities = 65/299 (21%), Positives = 125/299 (41%), Gaps = 34/299 (11%)

Query: 21  YALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEY-QGEYESLYT 79
           Y+ + C+ T E   +P+P+N+ + + N  ++L W     P E   +  ++ +  ++ +
Sbjct: 215 YSPVYCINTTERHKVPSPENIQINADNQIYVLKWD---YPYENATFQAQWLRAFFKKIPG 271

Query: 80  SHI--WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSILKHPFNRNSTI 137
           +H   W     C       C    ++++   Y +RVRA+ G+ TS WS  K       TI
Sbjct: 272 NHSDKWKQIPNCENVTSTHCVFPREVSSRGIYYVRVRASNGNGTSFWSEEKEFNTEMKTI 331

Query: 138 LTRPGMEIXK---XGFHLVI----ELEDLGPQ----FEFLVAYWXREPGAEEHVKMVRSG 186
           +  P + +        H+ +    E E++         + V +W     AE  V   R+
Sbjct: 332 IFPPVISVKSVTDDSLHVSVGASEESENMSVNQLYPLIYEVIFWENTSNAERKVLEKRTN 391

Query: 187 GIPVHLETMEPGAAYCVKAQTFVK--AIGXYSAFSQTECVXVQ----GEAIPLVLALFAF 240
            I      ++P   YCVKA+  ++       S+FS T C   +     +   +V    A
Sbjct: 392 FI---FPDLKPLTVYCVKARALIENDRRNKGSSFSDTVCEKTKPGNTSKTWLIVGTCTAL 448

Query: 241 VGFMLILVVVPLFVWKMGRLLQYSCCPVVVLPDTLK--ITNSPQK--LISCRREEVDAC 295
               +++ VV +F+    R ++Y   P    P ++    ++ P +  L+S   E+ + C
Sbjct: 449 FSIPVVIYVVSVFL----RCVKYVFFPSSKPPSSVDEYFSDQPLRNLLLSTSEEQTERC 503
```

```
>gi|6754302|ref|NP_034638.1|   (NM_010508) interferon (alpha and beta) receptor; IN
              [Mus musculus]
 gi|462416|sp|P33896|INR1_MOUSE   INTERFERON-ALPHA/BETA RECEPTOR ALPHA CHAIN PRECURS
              (IFN-ALPHA-REC)
 gi|284965|pir||A45283   interferon alpha/beta receptor - mouse
 gi|194112|gb|AAA37890.1|   (M89641) interferon alpha/beta receptor [Mus musculus]
          Length = 590

 Score = 47.8 bits (112), Expect = 2e-04
 Identities = 76/331 (22%), Positives = 138/331 (40%), Gaps = 29/331 (8%)

Query: 3   TFTMVLEEIWTSLFMWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGE 62
           T+ + ++ I  SL     Y+ + C+ T     +P P NL V +    ++L W   IA  +
Sbjct: 197 TYCLEVKAIHPSLKKHSNYSTVQCISTTVANKMPVPGNLQVDAQGKSYVLKWD-YIASAD 255

Query: 63  TVYYSVEYQGEYESLYTSHI--WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQ 120
            ++ +    G  +S   SH   W P   C+  +   C  + D   T  + L V+A+ G+
Sbjct: 256 VLFRAQWLPGYSKSSSGSHSDKWKPIPTCANVQTTHCVFSQDTVYTGTFFLHVQASEGNH 315

Query: 121 TSAWSILKHPFNRNSTILTRPGMEIXKXGFHLVIEL---EDLGPQFEFLVAYWXREPGAE 177
           TS WS  K   ++   +   P + +      L++ +   +       + + +W  E  +
Sbjct: 316 TSFWSEEKFIDSQKHILPPPPVITVTAMSDTLLVYVNCQDSTCDGLNYEIIFW--ENTSN 373

Query: 178 EHVKMVRSGGIPVHLETMEPGAAYCVKAQTFVKA-IGXYSAFSQTECVXVQGEAIPLVLA 236
             + M + G     L+ ++P   YCV+A+   +A +   S FS+  C   +  +   +
Sbjct: 374 TKISMEKDGP-EFTLKNLQPLTVYCVQARVLFRALLNKTSNFSEKLCEKTRPGSFSTIWI 432

Query: 237 LFAF-VGFMLILVVVPL-FVWKMGRLLQYSCCPVVVLPDTLK--ITNSPQK---LISCRR 289
           +    V F  ++V+  L  VWK    L + C P +  P ++    +  P K   L++
Sbjct: 433 ITGLGVVFFSVMVLYALRSVWKY---LCHVCFPPLKPPRSIDEFFSEPPSKNLVLLTAEE 489

Query: 290 --------EEVDACATAVM-SPEELLRAWIS 311
                    E  D  A  V  +PEE LR + S
Sbjct: 490 HTERCFIIENTDTVAVEVKHAPEEDLRKYSS 520
```

```
 Score = 42.7 bits (99), Expect = 0.006
 Identities = 38/201 (18%), Positives = 81/201 (39%), Gaps = 19/201 (9%)

Query: 35  LPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEG 94
            L  P+N+ V   +  + L WS       +V +S EY+ + E+      W+    C  T
Sbjct: 29  LKPPENIDVYIIDDNYTLKWSSHGESMGSVTFSAEYRTKDEAK-----WLKVPECQHTTT 83

Query: 95  PECDVT-DDITATVPYNLRVRATLGSQTSAWSILKHPFNRNSTILTRPGMEIXKXGFHLV 153
             +C+ +  D    +    RVRA  G+ TS+W+ +       +  ++ P + +      ++
Sbjct: 84  TKCEFSLLDTNVYIKTQFRVRAEEGNSTSSWNEVDPFIPFYTAHMSPPEVRLEAEDKAIL 143

Query: 154 IELEDLG----------PQFEFLVAYWXREPGAEEHVKMVRSGGIPVHLETMEPGAAYCV 203
            + +   G          P F + +  W +    +   K + S      +  + P   YC+
Sbjct: 144 VHISPPGQDGNMWALEKPSFSYTIRIWQKSSSDK---KTINSTYYVEKIPELLPETTYCL 200

Query: 204 KAQTFVKAIGXYSAFSQTECV 224
            + +    ++  +S +S  +C+
Sbjct: 201 EVKAIHPSLKKHSNYSTVQCI 221

>gi|20896187|ref|XP_128323.1|     (XM_128323) similar to interleukin 10 receptor 2 pr
            musculus]
           Length = 351

 Score = 47.4 bits (111), Expect = 2e-04
 Identities = 56/247 (22%), Positives = 103/247 (41%), Gaps = 34/247 (13%)

Query: 27  LLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPS 86
            LL   + ++P P+ + + S N K++L W     P   + ++ +Y+  Y S +  H
Sbjct: 15  LLVPALGMIPPPEKVRMNSVNFKNILQWEVPAFPKTNLTFTAQYE-SYRS-FQDH----- 67

Query: 87  SWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAW-SILKHPFNRNSTILTRPGMEI 145
              C  T   +CD +  ++    Y +RVRA L  + S W ++   P     TI+  P M+I
Sbjct: 68  --CKRTASTQCDFS-HLSKYGDYTVRVRAELADEHSEWVNVTFCPV--EDTIIGPPEMQI 122

Query: 146 XKXGFHLVIE--------------LEDLGPQFEFLVAYWXREPGAEEHVKMVRSGGIPVH 191
                  L +               L+++   + + V YW + G  E  ++V       V
Sbjct: 123 ESLAESLHLRFSAPQIENEPETWTLKNIYDSWAYRVQYW--KNGTNEKFQVVSPYDSEV- 179

Query: 192 LETMEPGAAYCVKAQTFVKAIGXYSAFSQTECVXVQGEAIPLVLALFAFVGFMLILVVVP 251
               +EP   YC++ Q F+        +S+  C     + I         V  +LI+ V+
Sbjct: 180 FGNLEPWTTYCIQVQGFLLDQNRTGEWSEPICERTGNDEITPSW----IVAIILIVSVLV 235

Query: 252 LFVWKMG 258
            +F++ +G
Sbjct: 236 VFLFLLG 242

>gi|163188|gb|AAA02571.1|   (L06320) alpha-interferon receptor [Bos taurus]
           Length = 560

 Score = 46.6 bits (109), Expect = 4e-04
 Identities = 46/204 (22%), Positives = 87/204 (42%), Gaps = 20/204 (9%)

Query: 21  YALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEY-QGEYESLYT 79
            Y+ + C+ T E   +P+P+N+ + + N  ++L W     P E   +  ++ +  ++ +
Sbjct: 215 YSPVYCINTTERHKVPSPENIQINADNQIYVLKWD---YPYENATFQAQWLRAFFKKIPG 271

Query: 80  SHI--WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSILKHPFNRNSTI 137
            +H   W     C       C   ++++    Y +RVRA+ G+ TS WS  K       TI
Sbjct: 272 NHSDKWKQIPNCENVTSTHCVFPREVSSRGIYYVRVRASNGNGTSFWSEEKEFNTEMKTI 331

Query: 138 LTRPGMEIXK---XGFHLVI----ELEDLGPQ----FEFLVAYWXREPGAEEHVKMVRSG 186
            +  P + +        H+ +    E E++         + V +W     AE  V   R+
Sbjct: 332 IFPPVISVKSVTDDSLHVSVGASEESENMSVNQLYPLIYEVIFWENTSNAERKVLEKRTN 391
```

```
Query: 187 GIPVHLETMEPGAAYCVKAQTFVK 210
             I      ++P   YCVKA+  ++
Sbjct: 392 FI---FPDLKPLTVYCVKARALIE 412
```

>gi|2612835|gb|AAB84231.1| (U65978) interferon alpha/beta receptor-1 [Ovis aries]
Length = 560

Score = 46.2 bits (108), Expect = 4e-04
Identities = 66/300 (22%), Positives = 113/300 (37%), Gaps = 36/300 (12%)

```
Query: 21  YALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTS 80
           Y+ + C+ T E   +P+P+N+ +   N  ++L W       +  Y S  +Q ++   +
Sbjct: 215 YSPVYCINTTERHKVPSPENVQINVDNQAYVLKW-------DYPYESTTFQAQWLRAFLK 267

Query: 81  HI-------WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSILKHPFNR 133
            I       W     C        C    DI +   Y +RVRA+ G+ TS WS   K  FN
Sbjct: 268 KIPGKHSNKWKQIPNCENVTTTHCVFPRDIFSMGIYYVRVRASNGNGTSFWSEEKE-FNT 326

Query: 134 NSTILTRPGM----EIXKXGFHLVI----ELEDLGPQ----FEFLVAYWXREPGAEEHVK 181
               +  P +     I     H+ +     E E++          + V +W     AE  V
Sbjct: 327 EVKPIIFPPVISMKSITDDSLHVSVGASEESENMSVNQLYPLVYEVIFWENTSNAERKVL 386

Query: 182 MVRSGGIPVHLETMEPGAAYCVKAQTFVK--AIGXYSAFSQTECVXVQGEAIPLVLALFA 239
             R+          ++P   YCVKA+  ++        S++S T C   +          +
Sbjct: 387 EKRTD---FTFPNLKPLTVYCVKARALIENDRWNKGSSYSDTVCEKTKPGNTSKTWLIAG 443

Query: 240 FVGFMLILVVVPLFVWKMGRLLQYSCCPVVVLPDTLKITNSPQK----LISCRREEVDAC 295
              +  ++VV    V     R ++Y    P     P ++    S Q      L+S   E+ + C
Sbjct: 444 ICTALFSILVVIYVVRVFLRCVKYVFFPSSKPPSSVDQYFSDQPLRNLLLSTSEEQTERC 503
```

>gi|2494729|sp|Q28589|INR1_SHEEP INTERFERON-ALPHA/BETA RECEPTOR ALPHA CHAIN PRECUR
(IFN-ALPHA-REC) (INTERFERON ALPHA/BETA RECEPTOR-1)
gi|1213627|emb|CAA65183.1| (X95939) type I interferon receptor [Ovis aries]
Length = 560

Score = 46.2 bits (108), Expect = 4e-04
Identities = 64/300 (21%), Positives = 110/300 (36%), Gaps = 36/300 (12%)

```
Query: 21  YALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTS 80
           Y+ + C+ T E   +P+P+N+ +   N  ++L W       +  Y S  +Q ++   +
Sbjct: 215 YSPVYCINTTERHKVPSPENVQINVDNQAYVLKW-------DYPYESTTFQAQWLRAFLK 267

Query: 81  HI-------WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSILKHPFNR 133
            I       W     C        C    DI +   Y +RVRA+ G+ TS WS   K  FN
Sbjct: 268 KIPGKHSNKWKQIPNCENVTTTHCVFPRDIFSMGIYYVRVRASNGNGTSFWSEEKE-FNT 326

Query: 134 NSTILTRPGM----EIXKXGFHLVIELEDLGPQFE--------FLVAYWXREPGAEEHVK 181
               +  P +     I     H+ +   +   P F          + V +W     AE  V
Sbjct: 327 EVKPIIFPPVISMKSITDDSLHVSVSASEESENMSVNQLYPLVYEVIFWENTSNAERKVL 386

Query: 182 MVRSGGIPVHLETMEPGAAYCVKAQTFVK--AIGXYSAFSQTECVXVQGEAIPLVLALFA 239
             R+          ++P   YCVKA+  ++        S++S T C   +          +
Sbjct: 387 EKRTD---FTFPNLKPLTVYCVKARALIENDRWNKGSSYSDTVCEKTKPGNTSKTWLIAG 443

Query: 240 FVGFMLILVVVPLFVWKMGRLLQYSCCPVVVLPDTLKITNSPQK----LISCRREEVDAC 295
              +  ++VV    V     R ++Y    P     P ++    S Q      L+S   E+ + C
Sbjct: 444 ICTALFSILVVIYVVRVFLRCVKYVFFPSSKPPSSVDQYFSDQPLRNLLLSTSEEQTERC 503
```

>gi|6680373|ref|NP_032364.1| (NM_008338) interferon gamma receptor 2 [Mus musculu
gi|627892|pir||A49947 interferon gamma receptor beta subunit - mouse
gi|545842|gb|AAB30165.1| (S69336) interferon gamma receptor beta subunit; IFN-ga
chain; IFN-gamma R species-specific cofactor [Mus sp.]
gi|1710144|gb|AAC52938.1| (U69599) ifngr2 [Mus musculus]
Length = 332

```
 Score = 46.2 bits (108), Expect = 5e-04
 Identities = 62/219 (28%), Positives = 91/219 (41%), Gaps = 38/219 (17%)

Query: 30  DEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPSSWC 89
           D  + L AP N  +   N + +L W P  +P        V YQ EY         +I  SW
Sbjct: 24  DSFSQLAAPLNPRLHLYNDEQILTWEP--SPSSNDPRPVVYQVEYS-------FIDGSWH 74

Query: 90  SLTEGPEC-DVTD---DITA-------TVPYN--LRVRATLGSQTSAWSILKHPFNRNST 136
            L E P C D+T+   D+T           P+   LRVRA  G+ TS W  L+ PF
Sbjct: 75  RLLE-PNCTDITETKCDLTGGGRLKLFPHPFTVFLRVRAKRGNLTSKWVGLE-PFQHYEN 132

Query: 137 ILTRP--GMEIXKXGFHLVIELE---DL--GPQFEFLVAYWXREPGAEEHVK-MVRSGGI 188
           +   P   + +      LVI      D+  G  F++LV YW +    +E V+   +S  I
Sbjct: 133 VTVGPPKNISVTPGKGSLVIHFSPPFDVFHGATFQYLVHYWEKSETQQEQVEGPFKSNSI 192

Query: 189 PVHLETMEPGAAYCVKAQTFV----KAIGXYSAFSQTEC 223
              L  ++P   YC++ +  +    K I  +  S   C
Sbjct: 193 V--LGNLKPYRVYCLQTEAQLILKNKKIRPHGLLSNVSC 229
```

```
>gi|7657691|ref|NP_055247.1|  (NM_014432) interleukin 20 receptor, alpha; class II
          receptor ZCYTOR7 [Homo sapiens]
 gi|6013325|gb|AAF01320.1|AF184971_1  (AF184971) class II cytokine receptor ZCYTOR
          Length = 553

 Score = 45.8 bits (107), Expect = 6e-04
 Identities = 29/93 (31%), Positives = 47/93 (50%), Gaps = 7/93 (7%)

Query: 35  LPAPQNLSVLSTNMKHLLMWSPVIA-PGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTE 93
           LP P N++ LS NMK++L W+P     G  V Y+V+Y      +Y    W+  S C
Sbjct: 37  LPKPANITFLSINMKNVLQWTPPEGLQGVKVTYTVQY-----FIYGQKKWLNKSECRNIN 91

Query: 94  GPECDVTDDITA-TVPYNLRVRATLGSQTSAWS 125
              CD++ + +     Y  +V+A  G++ S W+
Sbjct: 92  RTYCDLSAETSDYEHQYYAKVKAIWGTKCSKWA 124
```

```
>gi|12732140|ref|XP_004438.2|  (XM_004438) interleukin 20 receptor, alpha [Homo sa
 gi|14031069|emb|CAC38375.1|  (AL135902) bA204P2.1.1 (interleukin 20 receptor alpha
          [Homo sapiens]
          Length = 553

 Score = 45.8 bits (107), Expect = 6e-04
 Identities = 29/93 (31%), Positives = 47/93 (50%), Gaps = 7/93 (7%)

Query: 35  LPAPQNLSVLSTNMKHLLMWSPVIA-PGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTE 93
           LP P N++ LS NMK++L W+P     G  V Y+V+Y      +Y    W+  S C
Sbjct: 37  LPKPANITFLSINMKNVLQWTPPEGLQGVKVTYTVQY-----FIYGQKKWLNKSECRNIN 91

Query: 94  GPECDVTDDITA-TVPYNLRVRATLGSQTSAWS 125
              CD++ + +     Y  +V+A  G++ S W+
Sbjct: 92  RTYCDLSAETSDYEHQYYAKVKAIWGTKCSKWA 124
```

```
>gi|14031070|emb|CAC38376.1|  (AL135902) bA204P2.1.3 (interleukin 20 receptor alpha
          [Homo sapiens]
          Length = 209

 Score = 45.4 bits (106), Expect = 9e-04
 Identities = 29/93 (31%), Positives = 47/93 (50%), Gaps = 7/93 (7%)

Query: 35  LPAPQNLSVLSTNMKHLLMWSPVIA-PGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTE 93
           LP P N++ LS NMK++L W+P     G  V Y+V+Y      +Y    W+  S C
Sbjct: 37  LPKPANITFLSINMKNVLQWTPPEGLQGVKVTYTVQY-----FIYGQKKWLNKSECRNIN 91

Query: 94  GPECDVTDDIT-ATVPYNLRVRATLGSQTSAWS 125
              CD++ + +     Y  +V+A  G++ S W+
Sbjct: 92  RTYCDLSAETSDYEHQYYAKVKAIWGTKCSKWA 124
```

```
>gi|6680389|ref|NP_032374.1|     (NM_008348) interleukin 10 receptor, alpha [Mus musc
  gi|20888213|ref|XP_125167.1|     (XM_125167) interleukin 10 receptor, alpha [Mus mus
  gi|3024007|sp|Q61727|I10R_MOUSE   Interleukin-10 receptor alpha chain precursor (IL
  gi|2137457|pir||A49667   interleukin-10 receptor - mouse
  gi|437616|gb|AAA16156.1|     (L12120) interleukin-10 receptor [Mus musculus]
          Length = 575

 Score = 45.1 bits (105), Expect = 0.001
 Identities = 31/109 (28%), Positives = 46/109 (41%), Gaps = 9/109 (8%)

Query: 35  LPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEG 94
            LP+P  +    +   +H+L W P+     E+ YY V  +        Y +  W      C    +
Sbjct: 26  LPSPSYVWFEARFFQHILHWKPIPNQSESTYYEVALKQ-----YGNSTWNDIHICRKAQA 80

Query: 95  PECDVT----DDITATVPYNLRVRATLGSQTSAWSILKHPFNRNSTILT 139
              CD+T    D    +  Y  RVRA   SQ S W+  +  F  +  ILT
Sbjct: 81  LSCDLTTFTLDLYHRSYGYRARVRAVDNSQYSNWTTTETRFTVDEVILT 129

>gi|20856437|ref|XP_136952.1|     (XM_136952) similar to bA204P2.1.1 (interleukin 20
            isoform 1) [Mus musculus]
          Length = 560

 Score = 43.9 bits (102), Expect = 0.002
 Identities = 51/222 (22%), Positives = 91/222 (40%), Gaps = 33/222 (14%)

Query: 23  LIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIA-PGETVYYSVEYQGEYESLYTSH 81
            L+PC+        LP P N++ LS NMK++L W+P  +  G  V Y+V+Y        +Y
Sbjct: 46  LVPCVFCG----LPKPTNITFLSINMKNVLHWNPPESLHGVEVTYTVQY-----FIYGQK 96

Query: 82  IWIPSSWCSLTEGPECDVTDDIT-ATVPYNLRVRATLGSQTSAWSILK--HPFNRN---- 134
             W+ +S C        CD++ + +      +V+A   ++ S W+   +  +PF
Sbjct: 97  KWLNASKCGSINRTYCDLSVETSDYEHQFYAKVKAIWEARCSEWAETERFYPFLETQVSP 156

Query: 135 ------------STILTRPGMEIXKXGFHLVIELEDLGPQFEFLVAYWXREPGAEEHVKM 182
                         S  LT P           H V  ++ + P  ++ V+ +  +           +
Sbjct: 157 PEVALTTGEKSISIALTAPEKWKRNPQDHTV-SMQQIYPNLKYNVSVYNTKSRRTWSQCV 215

Query: 183 VRSGGIPVHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTECV 224
              S  +   L  +EP   YCV  ++ V           SQ +C+
Sbjct: 216 TNSTLV---LSWLEPNTLYCVHVESLVPGPPRLPMPSQKQCI 254

>gi|10835183|ref|NP_000620.1|     (NM_000629) interferon (alpha, beta and omega) rece
            interferon-alpha receptor (HuIFN-alpha-Rec) [Homo
            sapiens]
 gi|124462|sp|P17181|INR1_HUMAN   Interferon-alpha/beta receptor alpha chain precurs
            (IFN-alpha-REC)
 gi|106790|pir||A32694   interferon alpha/beta receptor precursor - human
 gi|306914|gb|AAA52730.1|     (J03171) interferon-alpha receptor precursor [Homo sapi
          Length = 557

 Score = 43.1 bits (100), Expect = 0.005
 Identities = 67/306 (21%), Positives = 120/306 (38%), Gaps = 49/306 (16%)

Query: 21  YALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYT- 79
            Y+ + C+ T      LP P+N+ V   N  ++L W        +  Y ++ +Q ++    +
Sbjct: 215 YSPVHCIKTTVENELPPPENIEVSVQNQNYVLKW-------DYTYANMTFQVQWLHAFLK 267

Query: 80  ----SHI--WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSILKHPFNR 133
                +H+  W      C  +  +C   ++     Y LRV+A+ G+ TS WS
Sbjct: 268 RNPGNHLYKWKQIPDCENVKTTQCVFPQNVFQKGIYLLRVQASDGNNTSFWSEEIKFDTE 327

Query: 134 NSTILTRPGMEI--XKXGFHLVIE----------LEDLGPQFEFLVAYWXREPGAEEHVK 181
                 L  P  I      FH+ I            ++D    +E +  +W      AE  +
```

```
Sbjct: 328 IQAFLLPPVFNIRSLSDSFHIYIGAPKQSGNTPVIQDYPLIYEII--FWENTSNAERKII 385

Query: 182 MVRSGGIPVHLETMEPGAAYCVKAQ--TFVKAIGXYSAFSQTECVXVQGEAIPLVLALFA 239
             ++    V +  ++P   YCVKA+  T  + +   S FS   C   +          ++
Sbjct: 386 EKKTD---VTVPNLKPLTVYCVKARAHTMDEKLNKSSVFSDAVCEKTKPGNTS---KIWL 439

Query: 240 FVGFMLILVVVPLFVWKMGRLLQYSCCPVVVLPDTLKITNS--------PQK--LISCRR 289
              VG  + L  +P  ++     L+  C   V  P +LK ++S          P K  L+S
Sbjct: 440 IVGICIALFALPFVIYAAKVFLR--CINYVFFP-SLKPSSSIDEYFSEQPLKNLLLSTSE 496

Query: 290 EEVDAC 295
           E+++ C
Sbjct: 497 EQIEKC 502

>gi|16166194|ref|XP_048562.2|     (XM_048562) similar to interferon (alpha, beta and
          1; human interferon-alpha receptor (HuIFN-alpha-Rec)
          [Homo sapiens]
 gi|18255502|gb|AAH21825.1|AAH21825   (BC021825) Unknown (protein for MGC:24928) [Ho
          Length = 557

 Score = 42.7 bits (99), Expect = 0.005
 Identities = 67/306 (21%), Positives = 120/306 (38%), Gaps = 49/306 (16%)

Query: 21  YALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYT- 79
            Y+ + C+ T     LP P+N+ V   N  ++L W       +  Y ++ +Q ++   +
Sbjct: 215 YSPVHCIKTTVENELPPPENIEVSVQNQNYVLKW-------DYTYANMTFQVQWLHAFLK 267

Query: 80  ----SHI--WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSILKHPFNR 133
               +H+  W     C   +  +C    ++      Y LRV+A+ G+ TS WS
Sbjct: 268 RNPGNHLYKWKQIPDCENVKTTQCVFPQNVFQKGIYLLRVQASDGNNTSFWSEEIKFDTE 327

Query: 134 NSTILTRPGMEI--XKXGFHLVIE----------LEDLGPQFEFLVAYWXREPGAEEHVK 181
             L  P   I       FH+ I              ++D    +E +  +W     AE  +
Sbjct: 328 IQAFLLPPVFNIRSLSDSFHIYIGAPKQSGNTPVIQDYPLIYEII--FWENTSNAERKII 385

Query: 182 MVRSGGIPVHLETMEPGAAYCVKAQ--TFVKAIGXYSAFSQTECVXVQGEAIPLVLALFA 239
             ++    V +  ++P   YCVKA+  T  + +   S FS   C   +          ++
Sbjct: 386 EKKTD---VTVPNLKPLTVYCVKARAHTMDEKLNKSSVFSDAVCEKTKPGNTS---KIWL 439

Query: 240 FVGFMLILVVVPLFVWKMGRLLQYSCCPVVVLPDTLKITNS--------PQK--LISCRR 289
              VG  + L  +P  ++     L+  C   V  P +LK ++S          P K  L+S
Sbjct: 440 IVGICIALFALPFVIYAAKVFLR--CINYVFFP-SLKPSSSIDEYFSEQPLKNLLLSTSE 496

Query: 290 EEVDAC 295
           E+++ C
Sbjct: 497 EQIEKC 502

>gi|32672|emb|CAA42992.1|     (X60459) interferon alpha/beta receptor [Homo sapiens]
          Length = 557

 Score = 42.7 bits (99), Expect = 0.005
 Identities = 67/306 (21%), Positives = 120/306 (38%), Gaps = 49/306 (16%)

Query: 21  YALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYT- 79
            Y+ + C+ T     LP P+N+ V   N  ++L W       +  Y ++ +Q ++   +
Sbjct: 215 YSPVHCIKTTVENELPPPENIEVSVQNQNYVLKW-------DYTYANMTFQVQWLHAFLK 267

Query: 80  ----SHI--WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSILKHPFNR 133
               +H+  W     C   +  +C    ++      Y LRV+A+ G+ TS WS
Sbjct: 268 RNPGNHLYKWKQIPDCENVKTTQCVFPQNVFQKGIYLLRVQASDGNNTSFWSEEIKFDTE 327

Query: 134 NSTILTRPGMEI--XKXGFHLVIE----------LEDLGPQFEFLVAYWXREPGAEEHVK 181
             L  P   I       FH+ I              ++D    +E +  +W     AE  +
Sbjct: 328 IQAFLLPPVFNIRSLSDSFHIYIGAPKQSGNTPVIQDYPLIYEII--FWENTSNAERKII 385
```

```
Query: 182 MVRSGGIPVHLETMEPGAAYCVKAQ--TFVKAIGXYSAFSQTECVXVQGEAIPLVLALFA 239
             ++    V +  ++P   YCVKA+  T  + +   S FS   C   +          ++
Sbjct: 386 EKKTD---VTVPNLKPLTVYCVKARAHTMDEKLNKSSVFSDAVCEKTKPGNTS---KIWL 439

Query: 240 FVGFMLILVVVPLFVWKMGRLLQYSCCPVVVLPDTLKITNS--------PQK--LISCRR 289
             VG  + L  +P  ++      L+  C   V  P +LK  +S        P K  L+S   
Sbjct: 440 IVGICIALFALPFVIYAAKVFLR--CINYVFFP-SLKPSSSIDEYFSEQPLKNLLLSTSE 496

Query: 290 EEVDAC 295
           E+++ C
Sbjct: 497 EQIEKC 502

>gi|4028137|gb|AAD13670.1|  (AF082665) interferon alpha/beta receptor 2 [Gallus gal
          Length = 508

 Score = 42.0 bits (97), Expect = 0.009
 Identities = 65/265 (24%), Positives = 106/265 (39%), Gaps = 43/265 (16%)

Query: 38  PQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTSHI-WIPSSWCSLTEGPE 96
           P NL + S N +H+L W     P    YY V         LY+SH  W  +  CS    P
Sbjct: 37  PDNLQMTSNNFQHILSWRAHSDPTVPTYYRV--------LYSSHSNWKIAKQCSRIVQPF 88

Query: 97  CDVTDDI-TATVPYNLRVRATLGSQTSAWSILKHP----------FNRNSTI------L 138
           C++TDD    +  Y+  V++ +G++    S+L              FN +S +      +
Sbjct: 89  CNLTDDFQVVSDEYSAFVQSFVGTEVFNSSLLHFSPLSETFLGPPEFNLSSCVHCINITI 148

Query: 139 TRPGMEIXKXGFHLVIELEDLGPQFEFLVAYWXREPGAEEHVK---MVRSGGIPVHLETM 195
             P   + K G   ++ L D+  +  + +    R  G EEH +    V       + +E
Sbjct: 149 KLPPTHLRKNG--KLLSLFDIYNKVNYEIT--LRTVG-EEHKRSPEKVTEEPFSIVIEEL 203

Query: 196 EPGAAYCVKAQTFVKAIGXYSAFSQTECVXVQ--GEAIPLVLALFAFVGFMLILVVVPLF 253
           EP   YCV        ++  +S  S  +C+      E     + +   + F +ILVV+  
Sbjct: 204 YPNRNYCVSVMV-TASLNKHSIPSAWKCITTDSVAEKDYYGITIAGAICFSIILVVILKC 262

Query: 254 VWKMGRLLQYSCCPVVVLPDTLKIT 278
           +   G +L          LPDTL  T
Sbjct: 263 LHLGGYILHKKS-----LPDTLVFT 282

>gi|4028141|gb|AAD13677.1|  (AF082667) interferon alpha/beta receptor 2 [Gallus gal
          Length = 508

 Score = 41.6 bits (96), Expect = 0.010
 Identities = 29/92 (31%), Positives = 44/92 (47%), Gaps = 10/92 (10%)

Query: 38  PQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTSHI-WIPSSWCSLTEGPE 96
           P NL + S N +H+L W     P    YY V         LY+SH  W  +  CS    P
Sbjct: 37  PDNLQMTSNNFQHILSWRAHSDPTVPTYYRV--------LYSSHSNWKIAKQCSRIVQPF 88

Query: 97  CDVTDDI-TATVPYNLRVRATLGSQTSAWSIL 127
           C++TDD    +  Y+  V++ +G++    S+L
Sbjct: 89  CNLTDDFQVVSDEYSAFVQSFVGTEVFNSSLL 120

>gi|16418459|ref|NP_443194.1|  (NM_052962) class II cytokine receptor; interleukin
          protein [Homo sapiens]
 gi|15212828|gb|AAK85715.1|  (AY040567) interleukin 22-binding protein CRF2-10L [H
 gi|16304593|emb|CAC85635.1|  (AJ313162) soluble cytokine class II receptor, long i
          sapiens]
          Length = 263

 Score = 41.6 bits (96), Expect = 0.011
 Identities = 51/232 (21%), Positives = 83/232 (34%), Gaps = 43/232 (18%)

Query: 38  PQNLSVLSTNMKHLLMWSPVIA-PGETVYYSVEYQGEYE-SLYTSHIWIPSSW------- 88
           PQ +   S N  ++L W P  A  G +  Y V+Y+  +   S+ +SH      W
Sbjct: 31  PQRVQFQSRNFHNILQWQPGRALTGNSSVYFVQYKIMFSCSMKSSHQKPSGCWQHISCNF 90
```

```
Query: 89   -------------------CSLTEGPECDVTDDIT-ATVPYNLRVRATLGSQTSAWSILK 128
                               C  T+    CD+T + +     PY  RVRA       S WS+
Sbjct: 91   PGCRTLAKYGQRQWKNKEDCWGTQELSCDLTSETSDIQEPYYGRVRAASAGSYSEWSMTP 150

Query: 129 HPFNRNSTILTRPGMEIXKXGFHLVIELE--------------DLGPQFEFLVAYWXREP 174
                T +  P M I +    L++ L                     +    +E L    +
Sbjct: 151 RFTPWWETKIDPPVMNITQVNGSLLVILHAPNLPYRYQKEKNVSIEDYYELLYRVFIINN 210

Query: 175 GAEEHVKMVRSGGIPVHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTECVXV 226
               E+  K+          V +E + P ++YCV A+ +     +  S  S+  CV +
Sbjct: 211 SLEKEQKVYEGAHRAVEIEALTPHSSYCVVAEIYQPMLDRRSQRSEERCVEI 262
```

>gi|15988304|pdb|1J7V|R   Chain R, Human Il-10 IL-10r1 Complex
Length = 214

Score = 40.8 bits (94), Expect = 0.019
Identities = 31/106 (29%), Positives = 47/106 (44%), Gaps = 6/106 (5%)

```
Query: 35   LPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEG 94
            LP+P ++    +     H+L W+P+      E+  Y V             Y    W    S CS T
Sbjct: 5    LPSPPSVWFEAEFFHHILHWTPIPQQSESTCYEVALL-----RYGIESWNSISQCSQTLS 59

Query: 95   PECD-VTDDITATVPYNLRVRATLGSQTSAWSILKHPFNRNSTILT 139
             +    VT D+   +   Y   RVRA   GS+ S W++     F+ +    LT
Sbjct: 60   YDLTAVTLDLYHSNGYRARVRAVDGSRHSQWTVTNTRFSVDEVTLT 105
```

>gi|106794|pir||S17112   interferon alpha/beta receptor - human
Length = 545

Score = 40.8 bits (94), Expect = 0.021
Identities = 66/299 (22%), Positives = 120/299 (40%), Gaps = 47/299 (15%)

```
Query: 21   YALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYT- 79
            Y+ + C+ T      LP P+N+ V   N  ++L W        +  Y ++ +Q ++    +
Sbjct: 215 YSPVHCIKTTVENELPPPENIEVSVQNQNYVLKW-------DYTYANMTFQVQWLHAFLK 267

Query: 80   ----SHI--WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSILKHPFNR 133
                +H+   W      C    +  +C     ++       Y LRV+A+ G+ TS WS
Sbjct: 268 RNPGNHLYKWKQIPDCENVKTTQCVFPQNVFQKGIYLLRVQASDGNNTSFWS---EEIKF 324

Query: 134 NSTILTRPGMEI-----XKXGFHLVIELEDLGPQFEFLVAYWXREPGAEEHVKMVRSGGI 188
            ++ I         I        + G   VI  +D     +E +   +W      AE   +     ++
Sbjct: 325 DTEIQVSDSFHIYIGAPKQSGNTPVI--QDYPLIYEII--FWENTSNAERKIIEKKTD-- 378

Query: 189 PVHLETMEPGAAYCVKAQ--TFVKAIGXYSAFSQTECVXVQGEAIPLVLALFAFVGFMLI 246
             V +  ++P    YCVKA+  T  + +    S FS   C   +             ++  VG  +
Sbjct: 379 -VTVPNLKPLTVYCVKARAHTMDEKLNKSSVFSDAVCEKTKPGNTS---KIWLIVGICIA 434

Query: 247 LVVVPLFVWKMGRLLQYSCCPVVVLPDTLKITNS--------PQK--LISCRREEVDAC 295
            L  +P  ++     L+  C   V  P +LK ++S         P K  L+S   E+++ C
Sbjct: 435 LFALPFVIYAAKVFLR--CINYVFFP-SLKPSSSIDEYFSEQPLKNLLLSTSEEQIEKC 490
```

>gi|4504633|ref|NP_001549.1| (NM_001558) interleukin 10 receptor, alpha; Interleu
[Homo sapiens]
gi|3024000|sp|Q13651|I10R_HUMAN   Interleukin-10 receptor alpha chain precursor (IL
gi|2135511|pir||I56215   interleukin-10 receptor - human
gi|482803|gb|AAA17896.1| (U00672) interleukin-10 receptor [Homo sapiens]
gi|20380860|gb|AAH28082.1| (BC028082) interleukin 10 receptor, alpha [Homo sapie
Length = 578

Score = 40.0 bits (92), Expect = 0.036
Identities = 31/106 (29%), Positives = 47/106 (44%), Gaps = 6/106 (5%)

```
Query: 35   LPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEG 94
```

```
            LP+P ++    +     H+L W+P+     E+  Y V          Y     W    S CS T
Sbjct: 26   LPSPPSVWFEAEFFHHILHWTPIPNQSESTCYEVALL-----RYGIESWNSISNCSQTLS 80

Query: 95   PECD-VTDDITATVPYNLRVRATLGSQTSAWSILKHPFNRNSTILT 139
             +    VT D+   +  Y  RVRA  GS+ S W++     F+ +   LT
Sbjct: 81   YDLTAVTLDLYHSNGYRARVRAVDGSRHSNWTVTNTRFSVDEVTLT 126

>gi|20560751|ref|XP_006447.7|     (XM_006447) similar to Interleukin-10 receptor alph
           precursor (IL-10R-A) (IL-10R1) [Homo sapiens]
          Length = 578

 Score = 40.0 bits (92), Expect = 0.036
 Identities = 31/106 (29%), Positives = 47/106 (44%), Gaps = 6/106 (5%)

Query: 35   LPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEG 94
             LP+P ++    +     H+L W+P+     E+  Y V          Y     W    S CS T
Sbjct: 26   LPSPPSVWFEAEFFHHILHWTPIPNQSESTCYEVALL-----RYGIESWNSISNCSQTLS 80

Query: 95   PECD-VTDDITATVPYNLRVRATLGSQTSAWSILKHPFNRNSTILT 139
             +    VT D+   +  Y  RVRA  GS+ S W++     F+ +   LT
Sbjct: 81   YDLTAVTLDLYHSNGYRARVRAVDGSRHSNWTVTNTRFSVDEVTLT 126

>gi|11991877|gb|AAG42376.1|AF296666_1    (AF296666) type I interferon receptor 1e [Ov
          Length = 332

 Score = 39.7 bits (91), Expect = 0.044
 Identities = 29/112 (25%), Positives = 48/112 (41%), Gaps = 14/112 (12%)

Query: 21   YALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTS 80
             Y+ + C+ T E    +P+P+N+ +    N  ++L W      +  Y S  +Q ++    +
Sbjct: 215  YSPVYCINTTERHKVPSPENVQINVDNQAYVLKW-------DYPYESTTFQAQWLRAFLK 267

Query: 81   HI-------WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWS 125
             I       W     C        C    DI +   Y +RVRA+ G+ TS WS
Sbjct: 268  KIPGKHSNKWKQIPNCENVTTTHCVFPRDIFSMGIYYVRVRASNGNGTSFWS 319

>gi|15212830|gb|AAK85716.1|     (AY040568) interleukin 22-binding protein CRF2-10S [H
          Length = 130

 Score = 38.5 bits (88), Expect = 0.087
 Identities = 28/91 (30%), Positives = 40/91 (43%), Gaps = 7/91 (7%)

Query: 38   PQNLSVLSTNMKHLLMWSPVIA-PGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPE 96
             PQ +   S N  ++L W P   A  G +  Y V+Y+      +Y     W     C  T+
Sbjct: 31   PQRVQFQSRNFHNILQWQPGRALTGNSSVYFVQYK-----IYGQRQWKNKEDCWGTQELS 85

Query: 97   CDVTDDIT-ATVPYNLRVRATLGSQTSAWSI 126
             CD+T + +    PY  RVRA       S WS+
Sbjct: 86   CDLTSETSDIQEPYYGRVRAASAGSYSEWSM 116

>gi|20896935|ref|XP_139651.1|     (XM_139651) similar to INTERFERON-ALPHA/BETA RECEPT
           PRECURSOR (IFN-ALPHA-REC) [Mus musculus]
          Length = 179

 Score = 35.4 bits (80), Expect = 0.80
 Identities = 24/94 (25%), Positives = 42/94 (44%), Gaps = 11/94 (11%)

Query: 35   LPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYES---LYTSHIWIPSSWCSL 91
             L  P+N     T+ +  L WS          +  + + G++++    + +   W P   C+
Sbjct: 61   LEPPENGDACVTDNRFTLKWSS--------HGLLPFSGQWDSFNRISSRDKWKPIPTCAD 112

Query: 92   TEGPECDVTDDITATVPYNLRVRATLGSQTSAWS 125
             TEG  C+VTDDITATVPYNLRVRATLGSQTSAWS
Sbjct: 113  VQTTHCVFSQDTVYTGTFFLRVQASEGNHTSFWS 146
```

>gi|18547428|ref|XP_089078.1| (XM_089078) similar to interleukin-22 binding prote
sapiens]
Length = 423

Score = 35.4 bits (80), Expect = 0.85
Identities = 54/208 (25%), Positives = 89/208 (41%), Gaps = 25/208 (12%)

```
Query: 35  LPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEG 94
           L  PQN+++LS N    L W P +   + V Y V YQ    S  T   W     C+ T+
Sbjct: 24  LAPPQNVTLLSQNFSVYLTWLPGLGNPQDVTYFVAYQ----SSPTRRRWREVEECAGTKE 79

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Query: 100 TDDITATV--PYNLRVRATLGSQTSAWSILKHPFNRNSTILT 139
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Gapped
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S1: 41 (22.0 bits)
S2: 71 (32.0 bits)
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CUTTING EDGE

Cutting Edge: STAT Activation By IL-19, IL-20 and mda-7 Through IL-20 Receptor Complexes of Two Types[1]

Laure Dumoutier,* Caroline Leemans,* Diane Lejeune,* Sergei V. Kotenko,† and Jean-Christophe Renauld[2]*

IL-10-related cytokines include IL-20 and IL-22, which induce, respectively, keratinocyte proliferation and acute phase production by hepatocytes, as well as IL-19, melanoma differentiation-associated gene 7, and AK155, three cytokines for which no activity nor receptor complex has been described thus far. Here, we show that mda-7 and IL-19 bind to the previously described IL-20R complex, composed by cytokine receptor family 2–8/IL-20Rα and DIRS1/IL-20Rβ (type I IL-20R). In addition, mda-7 and IL-20, but not IL-19, bind to another receptor complex, composed by IL-22R and DIRS1/IL20Rβ (type II IL-20R). In both cases, binding of the ligands results in STAT3 phosphorylation and activation of a minimal promoter including STAT-binding sites. Taken together, these results demonstrate that: 1) IL-20 induces STAT activation through IL-20R complexes of two types; 2) mda-7 and IL-20 redundantly signal through both complexes; and 3) IL-19 signals only through the type I IL-20R complex. ***The Journal of Immunology,*** **2001, 167: 3545–3549.**

Recently, a family of other cytokines with limited homology to IL-10 have been described (1). The first IL-10 homolog was called melanoma differentiation-associated gene 7 (mda-7)[3] because its expression was up-regulated during the in vitro differentiation of a melanoma cell line (2). Although this protein shows 22% amino acid identity with IL-10, it was not originally recognized as a secreted protein, and its biological activities remain poorly understood. The mouse ortholog of mda-7 was identified recently as a Th2-specific cytokine and called FISP, for IL-4-induced secreted protein (3). Its rat counterpart, called mob5, was suggested to play a role in ras oncogene-mediated neoplasia (4).

The *IL10* and *MDA7* genes have been mapped on chromosome 1q31–32, in a region where two additional IL-10-related genes, *IL19* and *IL20*, also were located. Little is known about IL-19, except that this gene is expressed by LPS-activated monocytes (5). The biological activities of IL-20 have been studied by using transgenic mice overexpressing this cytokine. These mice are characterized by neonatal lethality with skin abnormalities, including aberrant epidermal differentiation reminiscent of psoriasis lesions in human (6). An IL-20R complex was described as a heterodimer of two orphan class II cytokine receptor subunits: corticotropin-releasing factor (CRF) 2–8, proposed to be renamed IL-20Rα, and DIRS1, designated IL-20Rβ (6).

In addition to the chromosome 1q31–32 cluster, two other IL-10-related cytokines, AK155 and IL-22, are located on human chromosome 12q15, near the IFN-γ gene. AK155 is known to be up-regulated by *Herpes saimiri* infection of T lymphocytes, but its activity and receptor remain unknown (7). IL-22 was described originally as an IL-9-inducible gene and called IL-TIF, for IL-10-related T cell-derived inducible factor (8). IL-22 activities include induction of the acute phase response in hepatocytes and are mediated through a heterodimeric receptor composed of the CRF2–9/IL-22R subunit and the β-chain of IL-10R (9–11). In addition to its cellular receptor, IL-22 binds to a secreted member of the class II cytokine receptor family, which was called IL-22BP, and appears to act as a natural IL-22 antagonist (12, 13).

Materials and Methods

Cell cultures and cytokines

HT-29 intestinal epithelial cells were grown in IMDM medium supplemented with 10% FCS, 0.55 mM L-arginine, 0.24 mM L-asparagine, and 1.25 mM L-glutamine. Human embryonic kidney (HEK) 293-EBV nuclear Ag cells were grown in DMEM medium supplemented with 10% FCS. IL-10 homologs were produced by transient expression in HEK293-EBNA cells by the Lipofectamine 2000 method (Life Technologies, Gent, Belgium). The coding sequences for mda-7, IL-19, and IL-22 were amplified by RT-PCR from RNA of T cells stimulated with anti CD3 Ab. The IL-20 coding sequence was amplified from skin RNA. These cDNAs were cloned into pCEP4 plasmid (Invitrogen, Groningen, the Netherlands) under the control of the CMV promoter. mda-7-Flag, IL-19-flag, IL-20-flag and IL-22-flag were generated from the pCEP4-cytokine constructs by mutating the STOP codon and introducing a sequence encoding a C-terminal flag: Gly-Gly-Gly-Asp-Tyr-Lys-Asp-Asp-Asp-Asp-Lys. The IL-22BP-Ig fusion cDNA was produced as described before (12). For Western blot analysis, 10 μl of HEK293 supernatant was mixed with Laemmli sample buffer and boiled for 5 min before SDS-PAGE and transfer onto a polyvinylidene difluoride membrane (Amersham, Arlington Heights, IL). The membrane

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[3] Abbreviations used in this paper: mda-7, melanoma differentiation-associated gene 7; CRF, cytokine receptor family; HEK, human embryonic kidney.

0022-1767/01/$02.00

was probed with biotinylated anti-flag Ab (25 μg/ml) and with streptavidin-HRP (1/5000; Amersham). An ECL detection kit (Amersham) was used for expression of chemiluminescence. The chemiluminescence signal was detected and quantified with a Kodak (Rochester, NY) Digital Science Image Station 440CF. Anti-phospho-STAT3 Western blots were performed as described previously (8).

The DIRS1/IL-20Rβ cDNA was amplified by RT-PCR from K562 leukemia cells and cloned into pCEP4 plasmid. The IL-22R cDNA was amplified by RT-PCR from the HepG2 hepatoma cell line before cloning into the pEF-BOSpuro expression vector (14). The CRF2–8/IL-20Rα cDNA was amplified by PCR from a human placenta cDNA library (Clontech Laboratories, Palo Alto, CA), and cloned into the pCDEF3 plasmid. Anti-IL-10Rβ and anti-flag Abs were purchased from Peprotech (London, U.K.) and from Sigma (Bornem, Belgium), respectively. To produce anti-hIL-22R Abs, we transfected P815 mastocytoma cells with the hIL-22R cDNA in the pEF-BOS plasmid before injection into DBA/2 mice. After rejection of the tumors, the sera of these mice had high titers of neutralizing anti-hIL-22R Abs and were used at a 1/500 dilution.

Luciferase assays

The cytokine response was assessed by measuring luciferase production by cells transfected with the pGRR5 construct, (provided by Dr P. Brennan, Imperial Cancer Research Fund, London, U.K.). This construct contains five copies of the STAT-binding site of the FcγRI gene inserted upstream from a luciferase gene controlled by the TK promoter. Transfections of HT29 and HEK293 cells were performed as follows.

HT-29 cells were electroporated (10^7 cells in 400 μl, 250 V, 192 Ω, 1200 μF) with 15 μg of pGRR5 and 15 μg of each receptor cDNA, separately or in combination. Transfected cells were seeded in 96-well plates, incubated for 5 h at 37°C, and then preincubated, or not, for 1 h with anti-IL-22R antiserum (1/500) or with anti-IL-10Rβ Abs (6 μg/ml). Next, the cells were stimulated with each cytokine for 2 h. Luciferase activity was measured with the Luclite plus Assay System kit (Canberra-Packard, Meriden, CT) with a Top Count microplate scintillation counter (Canberra-Packard).

HEK293-EBNA cells were seeded in 24-well plates (Nunc, Roskilde, Denmark) for 24 h. Transfections were conducted by using the Lipofectamine method (Life Technologies, Gent, Belgium), with 500 ng of plasmid encoding IL-22R, IL-20Rβ, or IL-20Rα and with 100 ng of pGRR5. As an internal control, we used 100 ng of pRL-TK vector (Promega, Madison, WI) containing the *Renilla* luciferase gene under the control of the TK promoter. After 20 h, transfected cells were stimulated with cytokines, and 2 h later, cells were pelleted and lysed. Luciferase activity was monitored with the Dual-Luciferase Reporter Assay System kit (Promega).

IL-22BP interaction assays

Specific interactions between IL-22BP and cytokine-flag fusion proteins were assessed directly or indirectly by ELISA, as follows. Reacti-Bind Maleic Anhydride Activated Polystyrene plates (Pierce, Rockford, IL) were coated overnight at 4°C with 12.5 μg/ml of anti-flag Ab in PBS. The plates were incubated 2 h at 37°C with 50 μl of cytokine-flag fusion proteins (HEK293 supernatants). A total of 10% of supernatant of IL-22BP-Ig was added for 2 h, and bound IL-22BP-Ig was detected by using anti-mouse IgG3 polyclonal Abs coupled to peroxidase (Southern Biotechnology Associates, Birmingham, AL). The enzymatic activity was measured as described previously (12). In the indirect assay, we tested the inhibitory effect of IL-10 homologs on the binding of IL-22BP to IL-22. For this purpose, IL-22BP-Ig (10%) was preincubated with IL-10 homologs 2 h before incubation with Reacti-Bind plates (Pierce) that had been coated with rIL-22 as described previously (12).

Results

STAT activation by IL-10 homologs in class II cytokine receptor-transfected cells

To characterize the interactions between IL-10 homologs and receptors belonging to the class II cytokine receptor family, we expressed mda-7, IL-19, IL-20, and IL-22 as fusion proteins with a C-terminal flag sequence by transient transfection of HEK293 cells. Protein production was checked by Western blot with an Ab specific for the flag peptide (Fig. 1*A*). HEK293 cells secreted mda-7, IL-19, and IL-22 proteins with a heterogeneous MW of 23–30 kDa, most likely resulting from glycosylation. The IL-20-flag protein is secreted as a single band with a size of ~18 kDa, suggesting that this cytokine is not glycosylated. Quantification of the chemiluminescence signal indicated that IL-19 and IL-22 were produced at a similar level, whereas IL-20 and mda-7 were produced 7-fold less.

These HEK293 supernatants were used to assess the interaction with class II cytokine receptors. A first set of experiments were performed in HT-29 cells, which endogenously express IL-22R and IL-10Rβ. STAT activation induced by IL-22 was monitored with the pGRR5 luciferase reporter (9). As shown in Fig. 1*B* (*top left*), these cells failed to respond to the other IL-10 homologs. When HT-29 cells were transfected with the IL-20Rβ cDNA, both mda-7 and IL-20 induced luciferase production. Interestingly, this effect was completely blocked by an anti-IL-22R antiserum, suggesting that mda-7 and IL-20 can activate STAT factors through a new IL-20R complex composed by IL-22R and IL-20Rβ (Fig. 1*B*, *bottom left*).

When cells were transfected with both IL-20Rα and IL-20Rβ cDNAs, they became responsive to mda-7, IL-20, and IL-19, and the luciferase production was not affected anymore by anti-IL-22R

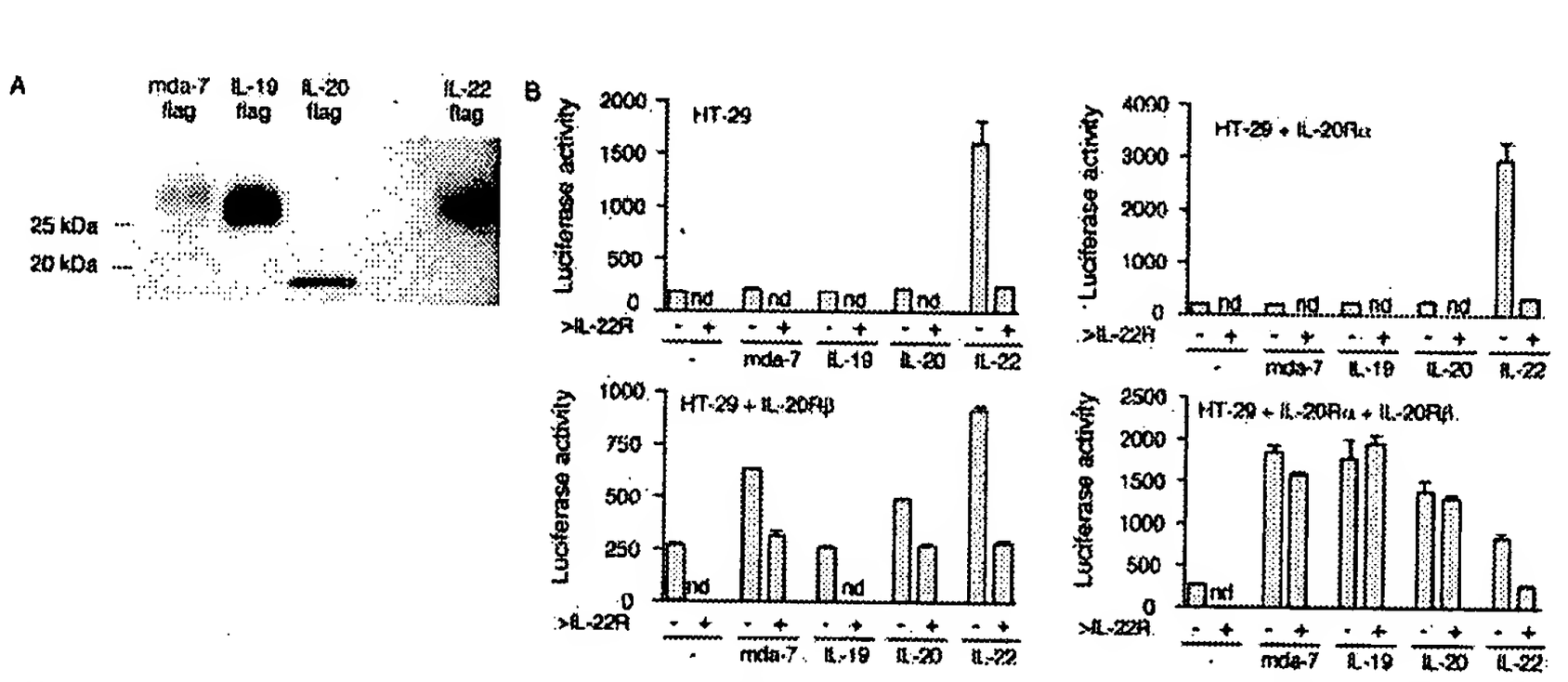

FIGURE 1. Human IL-10 homolog production and activity. *A*, The cDNAs encoding mda-7, IL-19, IL-20, and IL-22 tagged with a flag sequence were transfected in HEK293 cells. After 4 days, supernatants were analyzed by Western blotting with an Ab raised against the flag peptide. *B*, HT-29 cells were transfected with the pGRR5 luciferase construct with or without IL-20Rα and IL-20Rβ as indicated. Cells were preincubated 1 h with or without anti-IL-22R antiserum (1/500) before stimulation with 1% of HEK293 supernatants. Luciferase activity was monitored 2 h later and is expressed in arbitrary units.

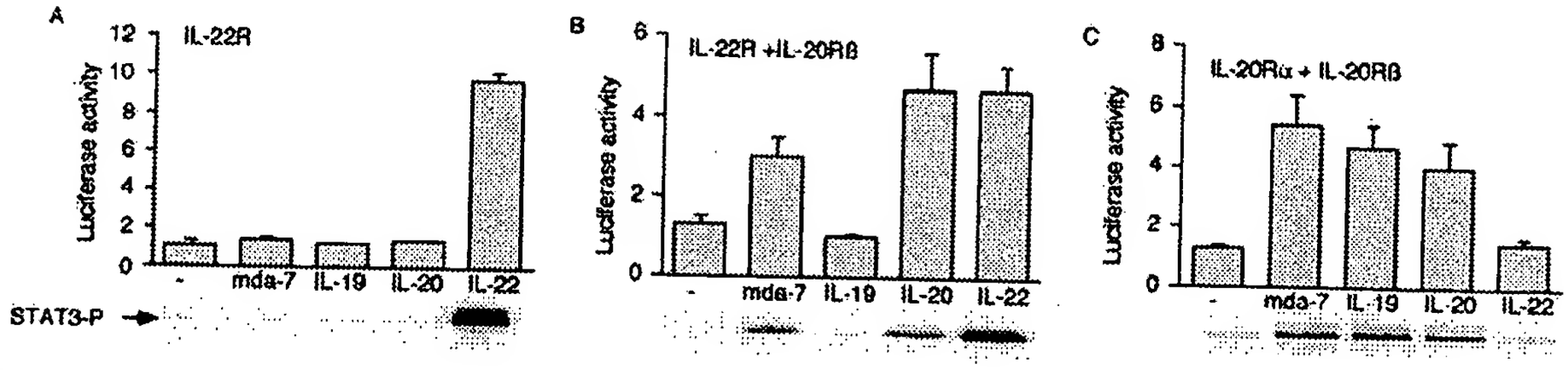

FIGURE 2. Activity of IL-10 homologs in HEK293 cells. HEK293 cells were transfected with the pGRR5 luciferase construct and cDNAs encoding IL-22R (*A*), IL-22R and IL-20Rβ (*B*), or IL-20Rα and IL-20Rβ (*C*). Cells were stimulated with 10% of mda-7, IL-19, IL-20, or IL-22 supernatant. Luciferase activity was monitored 2 h later. The results are normalized by using *Renilla* luciferase as an internal control. Western blot analysis for STAT3 phosphorylation was performed after 15 min of stimulation.

Abs (Fig. 1*B*, *bottom right*), indicating that this activity was independent from this chain. Finally, on transfection with the IL-20Rα cDNA alone, we failed to detect any response to mda-7, IL-19, and IL-20 (Fig. 1*B*, *top right*), confirming that IL-20Rβ is required for this process.

To characterize further the different types of receptor complexes, we used HEK293 cells, which express endogenous IL-10Rβ but not IL-22R. Untransfected HEK293 cells did not respond to any IL-10 homolog (data not shown). When the IL-22R cDNA was transfected, only IL-22 induced luciferase production and STAT-3 phosphorylation (Fig. 2*A*). Cells transfected with IL-22R and IL-20Rβ responded not only to IL-22 but also to IL-20 and mda-7 (Fig. 2*B*), whereas IL-20Rβ alone did not confer any cytokine responsiveness (data not shown). Transfection of both IL-20Rα and IL-20Rβ cDNAs allowed for STAT activation by mda-7, IL-19, and IL-20, but not IL-22 (Fig. 2*C*). No response was observed in cells transfected with the IL-20Rα cDNA alone (data not shown). In all cases, luciferase induction correlated with phosphorylation of STAT-3, as analyzed by Western blotting (Fig. 2). Similar results were obtained with HEK293 supernatants containing the wild-type cytokines.

Comparison of IL-20 and mda-7 sensitivity conferred by both types of IL-20R complexes

The observation that two different receptor complexes allowed for the response to IL-20 and mda-7 raised the possibility that each complex would respond preferentially to one cytokine. To test this hypothesis, we analyzed the response of HT-29 cells, transfected either with IL-20Rβ alone or both IL-20Rα and IL-20Rβ, to different dilutions of mda-7, IL-19, and IL-20 supernatants. When both IL-20Rα and IL-20Rβ were transfected, mda-7 and IL-20 dilutions showed a similar dose-response curve, indicating a similar sensitivity to both cytokines (Fig. 3, *bottom*). The activity of IL-19, but not those of mda-7 and IL-20, could be detected with 0.1% of supernatant, in agreement with the higher concentration of IL-19 supernatants. When only IL-20Rβ was transfected, HT-29 cells showed a better response to mda-7 at nonsaturating dilutions (1% and 0.1% supernatant), indicating that this type of complex is more sensitive to mda-7 (Fig. 3 *top*). Similar results were obtained in HEK293 cells (data not shown).

IL-20Rβ cannot substitute for IL-10Rβ in IL-22 signaling

The finding that IL-22R can associate not only with IL-10Rβ as described previously, but also with IL-20Rβ raised the possibility that the complex of IL-20Rβ with IL-22R could mediate an IL-22 response. Because IL-10Rβ is ubiquitously expressed, we could not address this question by direct transfection, but the role of IL-10Rβ was assessed with an anti-IL-10Rβ Ab. As shown in Fig. 4, this Ab could block the IL-22 activity both in control HT-29 cells and in cells transfected with the IL-20Rβ cDNA, indicating that IL-20Rβ cannot substitute for IL-10Rβ when the latter chain is not accessible to IL-22. The same Ab did not affect the activity of mda-7 or IL-20 in the same cells (data not shown).

mda-7, IL-19, and IL-20 do not bind IL-22BP

IL-22BP has been shown to bind IL-22 (12, 13), but nothing is known concerning its ability to bind other IL-10 homologs. The fact that this soluble receptor exhibits the same degree of homology with the extracellular domains of IL-22R and IL-20Rα prompted us to test the hypothesis that IL-22BP could also bind IL-20. In a first set of experiments, we tested the ability of the IL-10 homologs to compete for the binding of IL-22BP to insolubilized IL-22. Microtiter plates were coated with rIL-22 and incubated with an IL-22BP-Ig fusion protein in the presence of IL-10 homologs. The interaction between IL-22 and IL-22BP was detected with an anti-Ig Ab. As shown in Fig. 5*A*, only IL-22 supernatants were able to block IL-22BP binding. To directly assay the

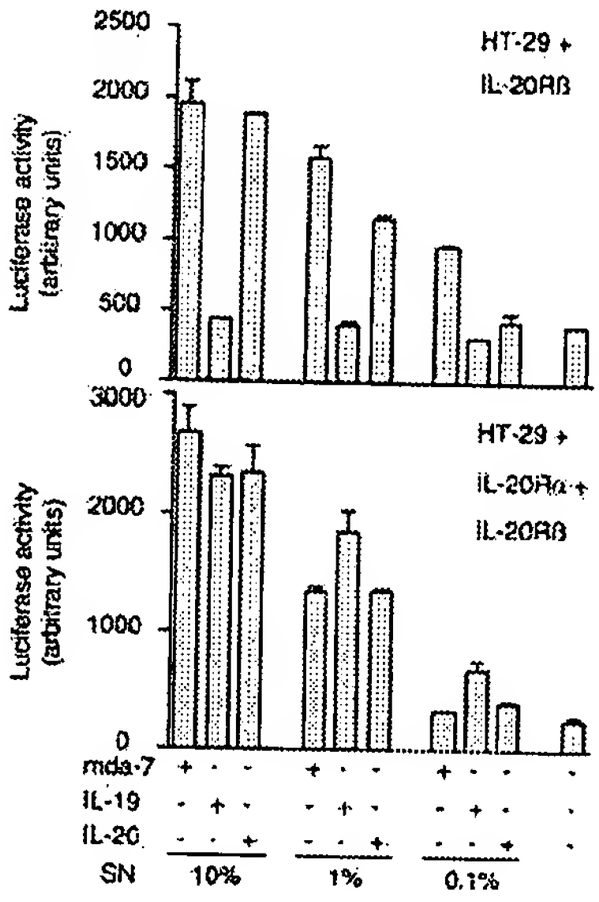

FIGURE 3. Comparison of IL-20 and mda-7 sensitivity with both types of IL-20R complexes. HT-29 cells were transfected with the pGRR5 luciferase construct and the cDNAs encoding IL-20Rβ alone (*top*), or IL-20Rα and IL-20Rβ (*bottom*). Cells were stimulated with different dilutions of mda-7, IL-19, and IL-20 supernatants for 2 h before measuring luciferase activity.

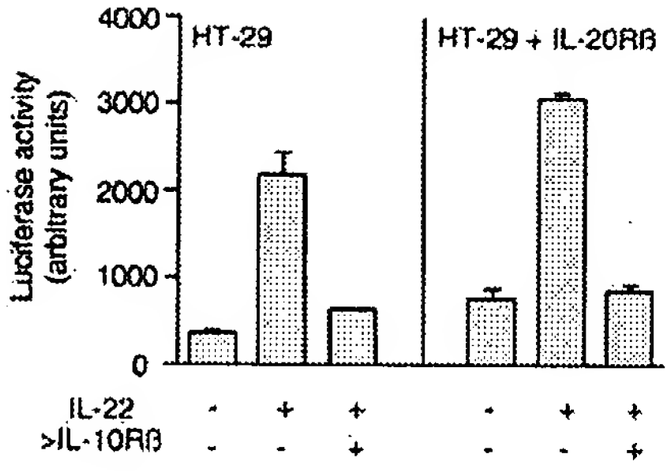

FIGURE 4. IL-20Rβ cannot substitute for IL-10Rβ in IL-22 signaling. HT-29 cells were transfected with the pGRR5 luciferase construct and the IL-20Rα cDNA. Cells were preincubated 1 h with anti-IL-10Rβ Ab before stimulation with 10% supernatant from IL-22- or mock-transfected HEK293. Luciferase activity was monitored 2 h later.

interaction between IL-10 homologs and IL-22BP, we coated microtiter plates with anti-flag Ab before incubation with flag-tagged IL-10 homologs. IL-22BP-Ig was added, and interaction was checked with an anti-Ig Ab. As shown in Fig. 5*B*, only IL-22 was able to bind IL-22BP-Ig, and no other IL-10 homolog showed the same activity.

Discussion

Sharing receptor subunits is a well-known feature within class I cytokine receptors and has allowed to define subfamilies based on the involvement of subunits such as βc, gp130, and IL-2Rγ. Among the class II cytokine receptors, the only example of a shared receptor so far was the IL-10Rβ chain, which is involved in both IL-10 and IL-22 signaling (9–11). In this paper, we show that IL-22R and DIRS1/IL-20Rβ are also shared by different receptor

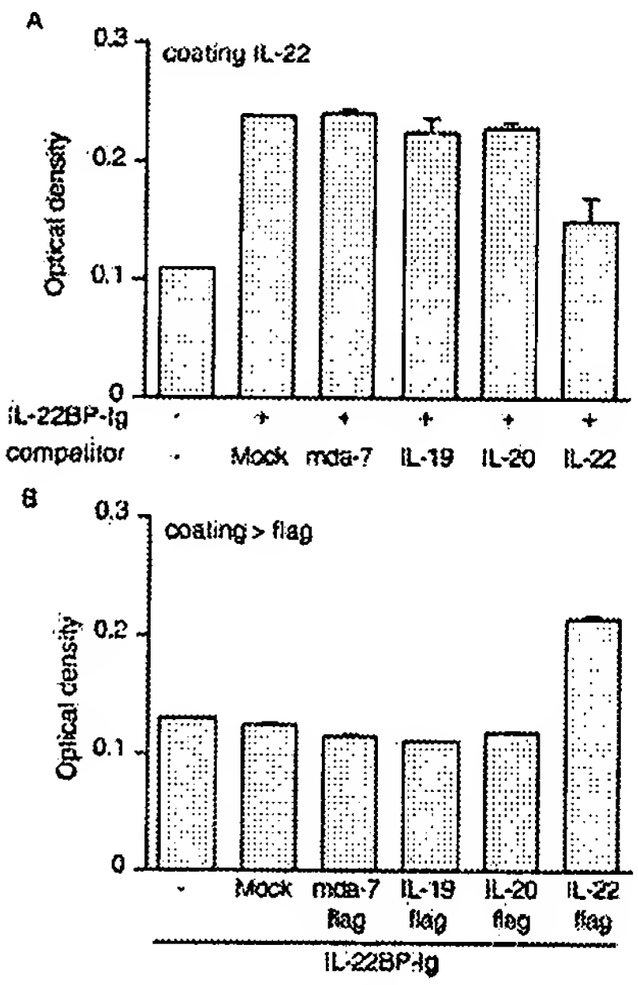

FIGURE 5. IL-22BP interacts specifically with IL-22. *A*, Plates were coated with rIL-22 before addition of IL-22BP-Ig preincubated with IL-10 homologs. Specific interactions were detected with rabbit polyclonal anti-Ig Abs. *B*, Plates were coated with anti-flag Ab. Supernatants containing flag-tagged IL-10 homologs were added before incubation with IL-22BP-Ig. Specific interactions were detected with a rabbit polyclonal anti-mouse Ig.

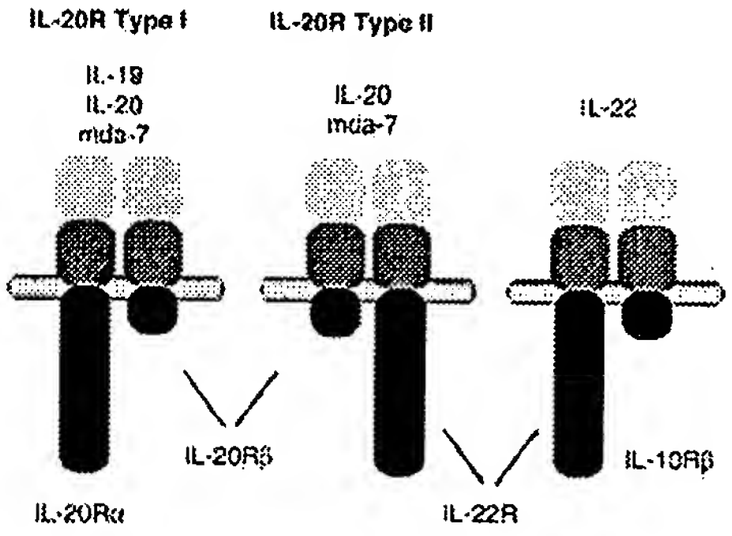

FIGURE 6. Schematic representation of IL-22R and IL-20R complexes.

complexes. The IL-20Rβ subunit can associate either with IL-20Rα, leading to a functional receptor for IL-19, IL-20, and mda-7 (type I IL-20R complex). IL-20Rβ also can associate with the IL-22R subunit and lead to a functional receptor for IL-20 and mda-7, but not for IL-19 (type II IL-20R complex), as schematically represented in Fig. 6. Additional experiments are needed to determine which of these chains serve as an actual ligand binding component or as a Jak-recruiting subunit. Alternatively, these receptor subunits may be expressed as preassociated complexes at the surface of the cells.

IL-20-transgenic mice show neonatal lethality and skin abnormalities, including thickened epidermis and expression of markers of hyperproliferation (6). Our observations strongly suggest that IL-19 and mda-7 can have a similar activity. Interestingly, IL-19 acts only on type I IL-20R and should therefore recapitulate only partly IL-20 activities. By contrast, IL-20 and mda-7 seem to behave similarly regarding both complexes. Noticeably, expression of the rat ortholog of mda-7 seems to be up-regulated during wound healing, a process that definitely involves keratinocyte proliferation (15).

Although mda-7 was originally identified several years ago (2), its activities and mode of action remain poorly understood. This protein was reportedly expressed intracellularly and was shown to induce apoptosis in certain tumor cell lines by an unknown mechanism (16, 17). On transfection of the mda-7 cDNA in HEK293 cells, we found most of the protein in the supernatant, indicating that it can be secreted, at least in this cell type. Secretion of the rat and mouse orthologs of mda-7 in various cell types also has been reported (3, 4). Together with our observation that exogenous mda-7 binds to the IL-20R complexes, these data support the hypothesis that mda-7 acts as a paracrine or autocrine factor. However, it remains possible that mda-7 might be expressed either as a cytoplasmic protein, inducing cell growth inhibition and apoptosis, or as a secreted protein acting on various cell types through IL-20R complexes.

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